

# Chapter 8

## Cardiovascular Diseases

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**INTRODUCTION.** An evaluation of the cardiovascular system is an essential part of any physical examination in large animals. Cardiovascular disorders can affect health, performance, production, and quality of life of the animal. Much of our current understanding of cardiac hemodynamics and heart sounds in domestic animals comes from large animal species.

**A.** History and **signalment.** The following information should be determined when presented with a patient:

1. Age
2. Sex
3. Environment
4. Management
5. Use of the animal
6. Problems with other animals in contact with the affected animal
7. Information on the animal's appetite, attitude, and symptoms
8. The time of onset of the current problem, attempted treatments, disease progression
9. Vaccination and deworming history, previous illnesses

**B.** Physical examination. A complete physical examination of all body systems is a necessary part of any thorough cardiovascular examination. One should note the animal's attitude, body weight, and body condition.

1. In order to determine the functional status of the cardiovascular system, one should examine the mucous membranes for color, moisture, and capillary refill time, and determine the amount of distention of the peripheral veins. The level of filling of the jugular vein and the patency of the vein should be determined. Peripheral arteries should be palpated for pulse quality and rhythm.
2. Evidence of edema along the ventral abdomen, sternum (brisket), submandibular area, and over the pectoral muscles should be sought. Edema of the limbs in horses and udder edema in cattle are less reliable signs of heart disease.
3. Auscultation is the most important part of the cardiovascular examination.
4. Cardiovascular sounds originate when the mechanical activity of the heart results in the sudden acceleration or deceleration of blood, causing the heart, major vessels, and blood to vibrate.
  - a. Types of heart sounds
    - (1) The first heart sound (**S1**) is caused by the initial ejection of blood from the ventricles, the closure of the atrioventricular (**AV**) valves, and the opening of the semilunar (**SL**) valves.
    - (2) The second heart sound (**S2**) is associated with closure of the **SL** valves, rapid reversal of blood flow (blood stops moving out of the heart), and opening of the **AV** valves.
    - (3) The third heart sound (**S3**) is associated with the end of the rapid filling of the ventricles with blood.
    - (4) The fourth heart sound (**S4**) is associated with atrial contraction. It is closely followed by **S1**.

TABLE 8-1. Typical Heart Rates in Adult Animals

Species	Typical Heart Rate (beats/min)
Horses	20–40
Cattle	60–80
Sheep and goats	70–90
Pigs	70–90

- b. In the various large animal species, there are differences in the number of heart sounds, the heart rate, and the rhythm.
  - (1) In sheep, goats, and pigs, only S1 and S2 are heard normally.
  - (2) In horses and cattle, all four heart sounds can be heard.
5. Heart rate. The heart rate in large animals varies depending on the animal's age and species (Table 8-1). Young animals tend to have a faster heart rate than adults. Sinus arrhythmias are common in normal sheep, goats, and young animals, but uncommon in adult cattle.
6. **Cardiac** murmurs are prolonged audible vibrations that occur during a normally silent period of the cardiac cycle. The exact mechanism resulting in the production of a heart murmur is unknown. Murmurs are classified according to timing, intensity, radiation, and quality. In some large animal species such as horses, cardiac murmurs and arrhythmias are extremely common. Thus, the interpretation of such findings should be made in the context of history, physical examination findings, and results of ancillary testing.
  - a. Pitch or frequency is the number of sound vibrations that occur within a unit of time. Heart sounds consist of a wide range of frequency components and are often not pure tones. However, murmurs may contain a fundamental pitch and overtones that produce a musical quality. Murmurs are described as low-, medium-, or high-pitched.
  - b. Quality is a subjective term that is determined by the murmur's frequency, amplitude, and duration. A murmur may be described as harsh, blowing, or squeaking. It can also be described as plateau (band-shaped), crescendo-decrescendo (diamond-shaped), decrescendo, crescendo, or continuous.
  - c. Intensity (amplitude) is the loudness of the cardiac murmur. Murmurs are quantified by a grading system (Table 8-2). A thrill is a fine vibration felt when the hand is placed over the patient's chest near the point of maximal intensity (PMI) of the heart murmur. It is associated with turbulent blood and the vibration is transmitted in the direction of blood flow. Loud heart murmurs (grades III–V or VI) often have a palpable thrill.

TABLE 8-2. Grading Scheme for Cardiac Murmurs in Large Animals

Grade of Murmur	Description of Murmur
Grade I	Barely audible, requires careful auscultation in a localized area of the chest to discern
Grade II	Faint, but clearly audible after listening to the chest for a few seconds
Grade III	Immediately audible over a wide area. A palpable thrill may accompany the murmur.
Grade IV	Very loud murmur. Heard with stethoscope lightly placed on chest wall. A palpable thrill may be present.
Grade V	Loudest audible murmur. Remains audible when the stethoscope is removed from direct contact with the chest wall. A pronounced thrill is always present.

- d. Timing and duration refers to whether the murmur occurs during systole, diastole, or is continuous. (Continuous murmurs encompass both systole and diastole.)
  - (1) Pansystolic murmurs encompass both S1 and S2.
  - (2) Holosystolic murmurs occur between S1 and S2.
  - (3) Holodiastolic murmurs are heard between S2 and S3.
  - (4) Presystolic murmurs are heard between S4 and S1.
- e. Radiation describes the location of the PMI of the murmur. This information helps determine the location of the underlying cardiac lesion. A murmur's radiation is often the direction of turbulent blood flow. Intense murmurs may radiate widely over the thorax.

- C. Ancillary tests for evaluating the cardiovascular system include electrocardiography, echocardiography, cardiac catheterization, and radiography. Successful diagnosis and management of cardiovascular diseases in large animals involves a proficiency with these diagnostic modalities and a familiarity with cardiac disease presentations, pathophysiology, and prevalence in specific large animal species.
  1. Electrocardiography records the electrical impulses that systematically flow through the heart and are responsible for cardiac contraction. The electrocardiogram (ECG) provides information about cardiac structure and function. Information such as the heart rate, rhythm, and conduction times can also be derived from ECG evaluation.
    - a. Technique. The base-apex lead is most commonly used. The positive lead is attached to the left fifth intercostal space at the PMI of the apex beat and the negative lead is attached to the right jugular furrow at the level of the base of the heart. The ground lead is attached away from the heart, usually on the dorsum. Leads should be attached to minimize interference due to movement of the animal or skin twitching.
    - b. Description of ECG. The form and direction of the electrocardiographic waves depend on the position of the heart, the course taken by the spread of electrical excitation throughout the myocardium, the position of the ECG recording leads, and the relative magnitude of the electrical forces during the cardiac cycle.
      - (1) Although large animals typically have very large hearts, measurement of the electrical impulses is difficult due to the size and shape of the thorax and the **multidirectionality** of depolarization. Therefore, the ECG can be used to diagnose arrhythmias in large animals, but is not useful in diagnosing disorders of chamber size.
      - (2) The multidirectionality of ventricular contraction in large animals is attributable to an extensive Purkinje fiber network that spreads throughout the ventricular myocardium, enabling explosive depolarization of all parts of the ventricle essentially at the same time. In contrast, small animals and people lack this extensive network and therefore, ventricular excitation occurs in three "fronts" or waves.
    - c. Indications. Many cardiac disorders can alter the morphology of the ECG recording in a diagnostically useful fashion. ECGs are particularly useful to characterize cardiac **arrhythmias**.
  2. Echocardiography is a safe, noninvasive way to assess chamber sizes, wall valve motion, wall thicknesses, and blood flow and intracardiac hemodynamics.
    - a. Types. There are three basic types of echocardiographic studies:
      - (1) M-mode echocardiography is useful for evaluating heart wall thickness, chamber diameters, and valve motion.
      - (2) **Two-dimensional (2D)** echocardiography is useful to depict anatomic relationships between cardiac structures and to define their movement relative to one another. 2D echocardiography is used to detect and display wall motion, abnormal communications, and intracardiac masses.
      - (3) Doppler echocardiography evaluates blood flow direction, turbulence, and velocity and allows estimation of pressure gradients within the heart and great vessels. Color-flow Doppler echocardiography converts the Doppler signals to an arbitrarily chosen color scale that represents the direction, velocity, and turbulence of blood semiquantitatively.

- b. Indications. Echocardiography helps identify and quantify the severity of valvular lesions, septal defects, intracardiac masses, cardiomyopathy, chamber hypertrophy, pericardial disease, aortic disease, and congenital heart disease.
3. Cardiac **catheterization**. An intravascular catheter is introduced through a peripheral vessel and passed into the heart.
  - a. Uses. Cardiac catheterization allows measurement of pressures in the blood vessels and heart chambers, as well as measurement of the oxygen tension, saturation, and content in the cardiac chambers. It also is used to assess cardiac output and vascular resistance. In contrast angiography, radiopaque material is injected and visualized using radiography in order to examine cardiovascular structures and blood flow.
  - b. Indications. Cardiac catheterization, an invasive technique, may be warranted if elevated artery pressures [such as occur with brisket disease, certain valvular abnormalities, shunts, and congestive heart failure (CHF)] are suspected.
4. Thoracic radiography
  - a. Use. Lateral radiographs are useful for detecting large changes in heart size and shape. Pulmonary pathology secondary to heart disease can be imaged.
  - b. Indications. Radiographic studies may be indicated if chamber or great vessel enlargement (especially dilatation) is suspected as a result of heart failure, valvular lesions, abnormal intracardiac and extracardiac communications (shunts), or some types of pulmonary disorders.

**D. Pathogenesis.** Heart failure occurs when heart disease from any cause becomes severe enough to overwhelm the compensatory mechanisms of the cardiovascular system. Mechanical inadequacy of the heart results in elevated venous and capillary pressures, leading to congestion and edema formation in the tissues, inadequate cardiac output, or both.

1. Left-sided heart failure most commonly manifests as pulmonary edema and signs of respiratory compromise (coughing and exertional dyspnea).
2. **Right-sided** heart failure manifests as ascites, tissue edema involving the brisket, submandibular, or ventral areas, liver congestion, prominent jugular distention, jugular pulsation, and weak arterial pulses. Over time, both right- and left-sided heart disease lead to generalized heart failure.
3. CHF. Signs of chronic heart failure referable to edema formation (i.e., pulmonary edema in left-sided heart failure, peripheral edema in right-sided heart failure) are called CHF. Because congestion and edema formation are the most common manifestations of chronic heart failure, the term CHF is often used synonymously with heart failure.

## II. BLOOD FLOW DISTURBANCES

**A.** Congenital cardiac diseases are abnormalities of cardiac structure or function that are present at birth. Proposed causes include maternal viral infections, use of pharmacologic agents, exposure to toxins, nutritional deficiencies in early pregnancy, and heredity. A variety of cardiovascular anomalies have been described in domestic animals.

1. Ventricular **septal defect** (VSD) is the most common congenital heart defect in horses and cattle.
  - a. Patient profile and history. VSD is reported in horses, cattle, small ruminants, and swine.
  - b. Clinical findings
    - (1) Animals with small defects may be clinically asymptomatic, except for the presence of a murmur.
    - (a) The usual murmur associated with VSD is grade III–IV, band-shaped, and

pansystolic with the PMI in the right third intercostal space at the heart base.

- (b) A similar murmur (usually one grade softer), caused by relative pulmonic stenosis, is auscultable at the base of the heart on the left side with the PMI over the pulmonic valve area.
- (c) Aortic insufficiency (i.e., the prolapse of the aortic valve leaflet into the septal defect during diastole due to lack of aortic root support) may cause a holodiastolic decrescendo murmur in the left third intercostal space.
- (2) Animals with large defects exhibit stunted growth, lethargy, dyspnea, exercise intolerance, and signs of CHF.
- c. Etiology and pathogenesis
  - (1) Etiology. Although the exact cause is unknown, possible causes include those listed in II A.
  - (2) Pathogenesis. Failure of the interventricular septum (often the membranous portion of the septum) to completely form in utero leads to the shunting of blood from the left ventricle to the right ventricle and right ventricular outflow tract after birth. This shunting increases the blood flow to the pulmonary circulation and increases the venous return to the left atrium and ventricle. Left atrial and ventricular dilatation occurs secondary to this volume overload, and left-sided CHF may occur.
- d. Diagnostic plan and laboratory tests. Diagnosis may be determined by several laboratory tests.
  - (1) Thoracic radiographs may reveal enlargement of the cardiac silhouette, prominence of the main pulmonary arteries (PA), and increased pulmonary vascular markings.
  - (2) **Echocardiography**. VSDs greater than 2 cm in diameter are visible on echocardiography. Left ventricular volume overload is also evidenced by a dilated left ventricle.
  - (3) Cardiac catheterization usually confirms increased oxygen saturation from the right atrium to PAs and increased pressures.
- e. Differential diagnoses
  - (1) Tetralogy of **Fallot** and other complex cardiac anomalies that include a VSD have similar auscultation findings. Cyanosis is often present at rest or following exertion with tetralogy.
  - (2) **Eisenmenger's** complex, which occurs when right ventricular pressure is high, causing the shunt accompanying a VSD to be from right-to-left, and is usually accompanied by cyanosis.
  - (3) Patent **ductus arteriosus** (PDA) may cause bilateral systolic murmurs, but a continuous murmur is more common.
- f. Therapeutic plan. There is no treatment for VSD. A palliative measure for correcting the intracardiac blood shunting associated with large VSDs is PA banding. This procedure has been used successfully in a small number of calves.
- g. Prognosis
  - (1) Small to moderate defects. Horses with defects that are smaller than 2.5 cm may have satisfactory athletic performance, whereas horses with moderately large defects may be used for pleasure only.
  - (2) Large defects. Horses with very large defects usually become stunted, exercise intolerant, and have a shortened life span.
2. Atrial **septal defect** (ASD)
  - a. Patient profile and history
    - (1) ASD has been reported in horses, cattle, small ruminants, and swine.
    - (2) The defect may occur in conjunction with other cardiac defects.
  - b. Clinical findings. Complaints may include fatigue, dyspnea on exertion, frequent respiratory tract infections, and symptoms associated with right ventricular failure.
    - (1) Small defects in the atrial septum may be clinically inapparent except for the presence of a cardiac murmur.
      - (a) Under low pressure, blood flows from the left atrium to the right atrium through the ASD, and the murmur results from increased volume being

ejected across the pulmonic valve. The murmur is usually a **holosystolic**, crescendo-decrescendo ejection murmur that is heard best over the left heart base.

- (b) An increased blood flow also may produce a diastolic murmur over the tricuspid valve.

(2) **Large defects.** If the ASD is large, right ventricular and left atrial dilation may occur. Pulmonary hypertension may result from irreparable changes in pulmonary vasculature due to the increased blood volume.

c. Etiology and pathogenesis

(1) Etiology. The cause of ASD is unknown. Proposed etiologies include those suggested in II A.

(2) Pathogenesis

(a) ASD results from the persistence of direct communication between the left and right atria after birth.

(i) **Ostium secundum** defect is the most common type of ASD defect. This defect occurs in the midportion of the intra-atrial septum following failure of the septum secundum to form properly. A patent foramen ovale is seen most frequently.

(ii) **Sinus venosus** type defect is associated with anomalous drainage of one or more pulmonary veins into the right atrium.

(b) The hemodynamic significance depends on the size of the defect and whether it is accompanied by other cardiac abnormalities. Typically blood moves from the left atrium into the right atrium because resistance is lower in the right heart chambers relative to the left atrium and ventricle. Volume overload of the right side of the heart results, causing right atrial, right ventricular, and PA dilatation.

d. Diagnostic plan and laboratory tests

(1) Thoracic radiographs reveal increased pulmonary blood flow, producing increased pulmonary vascular markings. Right ventricular enlargement is particularly apparent as reduced retrosternal lung fields in the lateral view. The PA may be enlarged.

(2) 2D echocardiography may show an enlarged right atrium, right ventricle, and left atrium. The ASD may be visualized if it is larger than 2 cm. Color-flow Doppler can demonstrate the shunt across the atrial septum.

(3) Cardiac catheterization. Diagnosis can be confirmed by the passage of a catheter across the ASD. Oxygen saturation is higher in the right atrium relative to normal.

e. Differential diagnoses

(1) Functional murmurs disappear with exertion, whereas the holosystolic murmur of ASD does not.

(2) Pulmonic **stenosis**. Cyanosis and polycythemia may occur in conjunction with holosystolic murmur.

(3) VSD often exhibits a bilateral systolic murmur.

(4) PDA may cause a systolic murmur on both sides of the thorax, but this condition more frequently causes a continuous murmur (see II A 3f).

f. Therapeutic plan and prognosis. There is no treatment for ASD. The prognosis is good if the animal is asymptomatic. In patients with pulmonary hypertension resulting in right ventricular failure, the prognosis is poor.

3. PDA

a. Patient profile. This disorder rarely occurs as a single defect in large animals, but it can occur in all large animal species.

b. Clinical findings

(1) Complaints may include stunted growth, exercise intolerance, signs of CHF, and cyanosis.

(2) Clinical signs depend on the length and diameter of the defect, the direction of the shunted blood, and the presence of other cardiac defects.

(a) The murmur is usually continuous and high pitched. It is heard over both sides of the thorax but is loudest on the left side of the thorax over the

aortic and pulmonic valve areas. Often there is a palpable continuous thrill over the third or fourth intercostal space on the left side. The murmur is referred to as a machinery murmur because it alternates intensity.

(b) Large defects. If the defect is very large, no murmur may be audible.

c. Etiology and pathogenesis

(1) Etiology. The reason for this defect is unknown. There is no evidence to suggest that PDA is hereditary in cattle or horses.

(2) Pathogenesis

(a) Normally, the ductus arteriosus closes in response to decreased pulmonary vascular resistance and increased systemic vascular resistance, which occurs at birth when breathing begins.

(i) Normal foals may have a PDA for a few days after birth, but closure should occur by 96 hours.

(ii) Normal ruminants rarely have a PDA after birth.

(b) PDA results from persistent patency of the fetal vessel that connects the pulmonary arterial system to the aorta (bypassing the lungs).

(i) With normal pulmonary vascular resistance, blood from the aorta is continuously shunted into the main PA (left-to-right shunt), resulting in excessive pulmonary blood flow and volume overload of the left atrium and left ventricle.

(ii) If pulmonary vascular resistance increases due to pulmonary vascular disease or pulmonary hypertension, blood may be shunted from the PA into the aorta (right-to-left shunt). This reversed PDA results in poorly oxygenated blood entering the systemic circulation, and differential cyanosis may result. With differential cyanosis, the cranial parts of the animal are well oxygenated, whereas the caudal parts are not.

d. Diagnostic plan and laboratory tests

(1) Thoracic radiographs may reveal an enlarged cardiac silhouette and prominent pulmonary markings. With left-sided heart failure, pulmonary venous congestion, interstitial pulmonary edema, and alveolar edema may be seen.

(2) Cardiac catheterization. A catheter usually can be passed from the PA into the descending aorta, confirming the presence of a PDA. The right ventricular and PA pressures and the PA oxygen saturation are elevated.

e. Differential diagnoses

(1) Complex cardiac **defect** with PDA as a component

(2) VSD. If the defect is very large, aortic insufficiency will result, causing a diastolic murmur in addition to the holosystolic murmur heard with a VSD.

(3) Vegetative endocarditis involving the AV or SL valves should not produce a continuous murmur.

f. Therapeutic plan

(1) Surgical repair is possible, but it is rarely economically feasible in large animal species.

(2) Pharmacologic closure of PDA with inhibitors of prostaglandin synthesis has been reported to be effective in people, but there is a risk of complications and recurrence. There are no reports of the efficacy of these drugs in large animals.

g. Prognosis. Animals with large defects have a poor prognosis because of the risk of CHF. It is not known whether small defects impair survival because they are often clinically undetectable and undiagnosed.

4. Tetralogy of Fallot

a. Patient **profile** and history. This disorder is reported in all large animal species but may be more common in calves than in foals.

b. Clinical findings

(1) Clinical signs often develop very early in life.

(a) Severe hypoxemia and cyanosis of the oral and nasal mucosae, tongue mucosa, and vaginal mucosa are present when hemoglobin is reduced by

more than 5 g/dl. Tetralogy of Fallot is one of the more common congenital cardiac defects in large animals that causes cyanosis.

- (b) Exercise intolerance is characterized by dyspnea, worsening cyanosis, and collapse.
- (c) Syncope, CHF, and sudden death also may occur.
- (2) Murmurs
  - (a) A loud systolic murmur (grade IV–V) may be transmitted widely over both thoracic walls.
  - (b) A systolic ejection murmur may be audible at the heart base over the aortic and pulmonic valve areas, whereas a harsh, more band-shaped **holo-**systolic murmur may be heard toward the apex of the heart. There may be a systolic thrill.
  - (c) With right ventricular hypertrophy and rising right ventricular pressure, the function of the tricuspid valve may be impaired and regurgitation may result. A systolic heart murmur that is loudest on the right side over the tricuspid valve may be heard.
- c. Etiology and pathogenesis
  - (1) Etiology. The cause of this complex heart defect is unknown. There is no evidence that this disorder is inherited. Proposed etiologies are listed in II A.
  - (2) Pathogenesis
    - (a) The abnormal development of the conal septum in the embryonic heart leads to the narrowing of the right ventricular infundibulum (i.e., pulmonary stenosis), an inability of the conal septum to participate in the closure of the interventricular foramen (**VSD**), and an overriding aorta. Right ventricular hypertrophy develops as a result of the pulmonary outflow obstruction. ASD may be present as well (pentalogy of Fallot).
    - (b) The degree of blood shunting is controlled by resistance across the stenotic right ventricular outflow tract as compared with resistance across the aortic valve. Blood moves from the right ventricle, through the VSD, into the aorta.
- d. Diagnostic plan and laboratory tests. Diagnosis is determined by the imaging and catheterization studies.
  - (1) Thoracic radiographs may reveal right ventricular enlargement and decreased pulmonary vasculature. The ascending aorta may be prominent, causing a loss of the cranial waist of the heart.
  - (2) Echocardiography may allow the visualization of the four components of the tetralogy. Color-flow Doppler can be used to characterize the abnormalities in blood flow and the severity of right ventricular outflow obstruction.
  - (3) Cardiac catheterization reveals equal pressure in the right and left ventricles. There is a pressure gradient between the right ventricle and the PA. Oxygen saturation is decreased in the left ventricle and aorta.
  - (4) Hematology. Packed cell volume and red blood cell (**RBC**) counts may be elevated over time due to chronic hypoxemia and blood sludging. In general, polycythemia is uncommon in foals with cyanotic cardiac disease and is usually present in less than 45% of calves.
- e. Differential diagnoses
  - (1) Respiratory distress syndrome of neonates. Tachypnea, dyspnea, cyanosis, and abnormal lung sounds are present, but there is no heart murmur.
  - (2) Central nervous system (**CNS**) dysfunction, such as neonatal maladjustment syndrome (**NMS**) and meningitis. Other neurologic signs are present, and there is no heart murmur.
  - (3) Heart failure with or without pulmonary edema or respiratory disease. With this disorder, there is improvement in cyanosis after supplementation with intranasal oxygen.
  - (4) Reversed PDA (right-to-left shunt) or VSD. These defects may cause differential cyanosis.
  - (5) Tricuspid or right ventricular atresia. The murmur of tricuspid insufficiency is holosystolic and is heard best along the right cardiac apex.

(6) Aortic anomalies. A diastolic murmur is heard best over the fourth intercostal space on the left side.

- f. **Therapeutic** plan and prognosis. There is no treatment for this condition, and the prognosis for long-term survival is poor.

## B. Acquired valvular diseases

1. Introduction. Disorders of any of the four cardiac valves commonly result in valve insufficiency.
  - a. Etiology and pathogenesis. Acquired valvular disorders result from degenerative changes, infection (bacterial or viral), inflammation, trauma, or unknown causes. With infectious or inflammatory conditions, vegetative lesions form on the cardiac valves, resulting in vegetative valvular **endocarditis**.
  - b. Clinical findings. Acquired valvular diseases are usually manifested by a cardiac murmur associated with valve incompetence. The murmur is heard over the affected valve and radiates in the direction of the regurgitant blood flow.
2. Left **AV** valve insufficiency (mitral regurgitation)
  - a. Patient profile. This condition is reported in all large animal species and occurs more commonly in horses than cows.
  - b. Clinical findings
    - (1) Complaints include intermittent fever, dyspnea, tachycardia, poor return to resting respiratory rate after exercise, coughing, and signs of CHF.
    - (2) Clinical signs associated with CHF may be present, including dyspnea due to pulmonary congestion and tissue edema.
    - (3) The murmur is usually grade III or higher. The murmur is holosystolic and is heard best over the mitral valve area (i.e., left side, fifth intercostal space in horses, fourth intercostal space in ruminants). The sound radiates dorsad and somewhat caudad, dorsal to the mitral valve area.
- c. Etiology and pathogenesis
  - (1) Etiology. Insufficiency of the mitral valve is caused by a deformation of the mitral valve cusps, dilation of the ventricles or valve ring, rupture of the chordae tendineae, or papillary muscle dysfunction. Possible causes for these defects are listed in II B 1 a.
  - (2) Pathogenesis
    - (a) When the mitral valve is unable to close completely, blood flows back into the left atrium during systole, causing volume overload and hypertrophy of the left atrium, endocardial damage to the atrial wall (**jet lesions**), and occasionally a full thickness tear in the left atrium.
    - (b) The mitral valve leak also initially leads to a decreased amount of blood pushed forward into the aorta.
    - (c) Eventually, left-sided heart failure ensues.
- d. Diagnostic plan and laboratory tests
  - (1) **Thoracic** radiographs may show cardiac enlargement, pulmonary venous distention, pulmonary edema, or pulmonary vascular congestion.
  - (2) Echocardiography may reveal a vegetative lesion on the mitral valve or prolapse of the mitral valve into the left atrium during systole. A normal to increased shortening fraction may be noted in conjunction with the murmur. Left-sided heart enlargement may be apparent. Color-flow Doppler may reveal the regurgitant blood during systole.
  - (3) Cardiac catheterization. A pulmonary capillary wedge tracing usually shows a large v pressure curve. If radiopaque **dye** is placed in the left ventricle, it will move into the left atrium during **systole**.
  - (4) Tests to screen for bacterial endocarditis (**BE**) [see II B 6 d] should also be performed.
- e. Differential diagnoses
  - (1) Primary respiratory disease. No heart murmur is present with this condition.
  - (2) Neurologic disorders, such as meningitis, encephalitis, and encephalopathy. Other neurologic signs may be present in the absence of a heart murmur.
  - (3) Dilated cardiomyopathy. Echocardiography can be used to distinguish

dilated cardiomyopathy from left AV valve insufficiency. With dilated cardiomyopathy, echocardiography reveals right and left ventricular chamber enlargement with ? decreased ventricular shortening fraction. Thoracic radiographs may also reveal generalized cardiomegaly.

- f. Therapeutic plan. For patients with vegetative lesions, treatment consists of the long-term administration of antimicrobials (see II B 6 f). The use of diuretics and anticoagulants may provide some symptomatic relief.
  - g. Prognosis depends on the severity of the mitral valve defect and the age of the patient. If the patient develops CHF, the prognosis is poor.
3. Right AV valve insufficiency (tricuspid regurgitation)
    - a. Patient profile. This condition occurs in all large animal species, but it is more common in cattle than horses.
      - (1) In one report, tricuspid regurgitation murmurs occurred in 16.4% of National Hunt racing Thoroughbreds and 3.7% of nonracing Thoroughbreds.
      - (2) In cattle, the tricuspid valve is the most common site for vegetative valvular endocarditis lesions.
    - b. Clinical findings
      - (1) Complaints may include exercise intolerance, weight loss, intermittent fever, and weakness.
      - (2) Physical examination findings can include a positive jugular venous pulse wave during ventricular systole, syncope, ascites, venous distention, and pulmonary hypertension in addition to the characteristic heart murmur.
        - (a) Right-sided **holosystolic** murmurs compatible with tricuspid regurgitation are the most common murmur reported in athletic horses, although post-mortem lesions involving the tricuspid valve are not always present in those horses.
        - (b) The holosystolic murmur associated with tricuspid regurgitation is heard best over the tricuspid valve area (right cardiac apex). A precordial thrill may be palpable.
    - c. Etiology and pathogenesis
      - (1) Etiology [see II B 2 c (1)]. Tricuspid regurgitation in horses occurs frequently in combination with mitral regurgitation and is caused by left-sided heart failure and pulmonary hypertension.
      - (2) Pathogenesis. With the inability of the tricuspid valve to close during systole, blood flows back into the right atrium. Chamber dilation and jet lesions (i.e., damage to the endocardium by a stream of regurgitant blood moving with a high velocity through an incompetent valve) on the atrial wall may result, and right-sided heart failure occurs over time.
    - d. Diagnostic plan and laboratory tests
      - (1) Thoracic radiographs reveal right-sided heart enlargement.
      - (2) **Echocardiography** may reveal a vegetative lesion on the tricuspid valve, valve thickening or shortening, or prolapse of the valve leaflets into the right atrium during systole. A normal to increased shortening fraction may be noted in conjunction with the murmur. Right ventricular volume overload and right atrial enlargement may be apparent. **Color-flow** Doppler may show the regurgitant blood during systole.
      - (3) Cardiac catheterization. Radiopaque dye placed in the right ventricle will be seen in the right atrium before it appears in the pulmonary vasculature.
      - (4) **Diagnostic** tests to screen for BE (II B 6 d) should also be performed.
    - e. **Differential** diagnoses
      - (1) VSD. VSD can be distinguished from tricuspid regurgitation using echocardiography.
      - (2) Mitral stenosis and tricuspid regurgitation may occur concurrently.
      - (3) Dilated cardiomyopathy can be distinguished from tricuspid regurgitation using echocardiography.
      - (4) Primary respiratory disease may cause similar clinical findings, including exercise intolerance and coughing, but no heart murmur is present.

f. Therapeutic plan and prognosis are the same as for left AV valve insufficiency (see II B 2 f–g).

4. Aortic valve insufficiency
  - a. Patient profile and history. This disorder can occur in all large animal species, but it is particularly common in older horses.
  - b. Clinical findings
    - (1) Complaints. Usually aortic regurgitation is well tolerated and is not associated with exercise intolerance. However, performance may be impaired.
    - (2) Physical examination findings
      - (a) Murmur
        - (i) Location. The murmur associated with aortic regurgitation is **holodiastolic** with the PMI over the aortic valve (fourth intercostal space on the left side in horses, third intercostal space in ruminants) and radiating toward the left cardiac apex.
        - (ii) Characteristics. The murmur usually begins at the time of S2 and is generally decrescendo in shape. Sometimes the murmur waxes and wanes in intensity, exhibiting one or more peaks during diastole. It may have a honking quality. Occasionally, atrial contraction may interrupt the aortic diastolic murmur or increase the intensity of the murmur.
      - (b) In severe cases, bounding arterial pulses may be present, indicating diastolic runoff and left ventricular volume overload.
      - (c) Signs of CHF may develop rapidly (e.g., jugular venous distention, subcutaneous edema, ascites, respiratory distress).
      - (d) Atrial **dysrhythmias**, most frequently atrial fibrillation (AF), often develop secondary to atrial enlargement.
    - c. Etiology and pathogenesis
      - (1) Etiology. Possible causes are enumerated in II B 1 a.
      - (2) Pathogenesis. With aortic insufficiency, blood flows from the aorta to the left ventricle through the incompetent valve during diastole. The murmur is associated with leakage of blood back into the left ventricle.
        - (a) Initially, the left ventricle cannot accommodate the large blood volume, resulting in elevated pressure in the left atrium and pulmonary circulation.
        - (b) Over time, the left ventricle undergoes compensatory changes to accommodate the increased blood flow by dilatation and hypertrophy. With chronicity, there is progressive fibrosis of the left ventricle, which consequently leads to myocardial dysfunction.
        - (c) The severity of aortic regurgitation depends on the size of the regurgitant aortic orifice, the pressure gradient across the aortic valve during diastole, and the duration of diastole. Common changes associated with the aortic valve include fibrotic bands, especially along the free edge of the aortic valve cusps at the site of valve closure, and vegetative lesions on the valve itself.
    - d. Diagnostic plan and laboratory tests
      - (1) Thoracic radiographs reveal left-sided heart enlargement.
      - (2) Echocardiography may reveal a vegetative lesion on the aortic valve, nodules or fibrotic plaques on the valve resulting in valve thickening or shortening, or the prolapse of the valve leaflets into the left atrium during diastole. Left ventricular volume overload and left atrial enlargement may be apparent. **Color-flow** Doppler may show the regurgitant blood during diastole. Impaired left ventricular function is noted.
      - (3) Diagnostic tests to screen for BE should also be performed (see II B 6 d).
    - e. **Differential** diagnoses
      - (1) **Pulmonic** regurgitation can be distinguished from aortic valve insufficiency using echocardiography.
      - (2) **Mitral** or tricuspid valve stenosis. In these disorders, the murmur is heard best during mid- to late diastole and is often loudest at the end of diastole.

The murmur associated with aortic regurgitation is heard in early diastole and is decrescendo in shape.

- (3) **Hyperdynamic** states (e.g., those induced by fever, anemia, and exercise) can cause a diastolic murmur as increased blood flow moves across the normal AV valves.

f. Therapeutic plan. No treatment is necessary if affected animals are asymptomatic. If there are symptoms, therapy is the same as for AV valve insufficiency (see II B 2 f).

g. Prognosis is good if the animal is asymptomatic. If the disorder is caused by **BE** or if signs of CHF develop, the prognosis is poor.

5. **Pulmonary valve insufficiency** is the least common valvular disease in young athletic racehorses and horses that are presented for slaughter.

a. Patient profile. Although uncommon, this disorder can occur in all large animals.

b. Clinical finding. This condition may develop in horses with pulmonary hypertension and CHF but is rarely detected clinically.

- (1) Complaints may include severe exercise intolerance, intermittent fever, weight loss, anorexia, or signs of CHF.
- (2) The characteristic murmur associated with pulmonic regurgitation is a holosystolic murmur that is heard best over the left heart base in the third intercostal space in horses and the second intercostal space in cattle (i.e., the pulmonic valve region). The murmur may radiate along the pulmonic outflow tract.

c. Etiology and pathogenesis

- (1) Etiology. In large animals, **BE** and trauma may cause the primary lesions of the pulmonic valve that result in regurgitation. In cattle, high altitudes may also cause pulmonary valve insufficiency.
- (2) Pathogenesis. The insufficiency of the pulmonic valve allows the regurgitation of blood into the right ventricle during diastole. Severe pulmonary hypertension may lead to pulmonic regurgitation.

d. Diagnostic plan and laboratory tests

- (1) Thoracic radiographs may reveal right-sided heart enlargement, particularly right ventricular. If pulmonary hypertension is present, increased pulmonary vascular markings or pulmonary edema may be evident.
- (2) Echocardiography may show a vegetative lesion on the pulmonic valve or valvular dysfunction. Color-flow Doppler may reveal the regurgitant jet of blood during right ventricular systole. Enlargement of the right ventricle may be a parent because of volume overload.
- (3) Diagnostic tests to screen for **BE** should also be performed (see II B 6 d).

e. Differential diagnoses include aortic regurgitation and the differentials for aortic regurgitation.

f. Therapeutic plan and prognosis

- (1) Treatment depends on the etiology, onset, duration, and severity of the lesion. Treatment for **BE** (see II B 6 f) may be appropriate.
- (2) Prognosis. Generally, the prognosis is guarded to poor when there is clinical evidence of valvular incompetence (e.g., tachycardia, exercise intolerance, signs of CHF, evidence of cardiac chamber enlargement).

6. Bacterial **endocarditis** (**BE**)

a. Patient profile. Horses, swine, and cattle can be afflicted with **BE**.

- (1) Horses. In horses, **BE** is uncommon and males may be overrepresented.
- (2) Swine. **BE** occurs more commonly in swine than in other large animal species. Swine younger than 1 year are most often affected.
- (3) Cattle. **BE** is often undiagnosed or misdiagnosed in cattle; adult cattle are most often affected. Many affected cattle have a history of being treated for pneumonia, reticuloperitonitis, or other infectious diseases.

b. Clinical findings

- (1) Equine and porcine **BE**. Although swine may have clinical signs similar to those seen in horses, **BE** is more often a postmortem finding rather than a clinical condition in swine.

(a) Complaints are extremely variable but may include cyclic or intermittent fevers, weight loss, lameness, weakness, or anorexia.

(b) Physical examination findings

- (i) A heart murmur, associated with a vegetative lesion on one or more heart valves, is often present. In horses, the aortic valve is most commonly involved, followed by the mitral valve. Likewise, in swine, the left AV and SL heart valves are most frequently affected.
- (ii) Signs associated with CHF often develop. With left-sided heart failure (a sequela of aortic valve dysfunction), signs include **persistent** cough, pulmonary edema, syncope, and exercise intolerance.
- (iii) Signs of other common sequelae (e.g., thromboembolism, **nonseptic** arthritis, **embolic showers**) may also be seen. Embolic showers can lead to infarction or metastatic infection at distant organ sites (e.g., the myocardium, lungs, kidney, brain, retina, vertebral vasculature, or synovial membranes).

(2) Bovine **BE**

(a) Complaints may include shifting limb lameness, anorexia, weight loss, cough, diarrhea, and decreased milk production.

(b) Physical examination findings

- (i) A heart murmur is often detectable. Vegetative lesions most often involve the tricuspid valve.
- (ii) Signs of right-sided heart failure (e.g., tachycardia, jugular and mammary vein distention, jugular pulsation, ventral and submandibular edema) are also associated with tricuspid valve insufficiency.
- (iii) Other signs include fever (constant or intermittent), tachypnea, dyspnea, pale mucous membranes, and scleral injection.

c. Etiology and pathogenesis

(1) Etiology. Theoretically, any bacteria that gains access to the blood can colonize the heart valves and endocardium, resulting in **BE**.

(a) In horses, *Streptococcus equi* subspecies *zooepidemicus* and *Actinobacillus equi* are the most common causes.

(b) In swine, *Streptococcus* species and *Erysipelothrix rhusiopathiae* are the most common causes.

(c) In cattle, common causative agents include *Actinomyces pyogenes* and *Streptococcus* species.

(2) Pathogenesis

(a) Acute **BE**. The only predisposing factor necessary for the development of acute **BE** is infection with an organism that has the ability to bind to the heart valve endothelium directly. The most common organism capable of causing acute **BE** in all domestic animals is *Staphylococcus aureus*.

(b) Chronic (subacute) **BE**. The presence of four factors is necessary for the development of chronic **BE**: endocardial damage, the formation of a platelet-fibrin thrombus on the damaged endothelium, bacteremia, and a high agglutinating antibody titer toward the infecting organism.

d. Diagnostic plan and laboratory tests

(1) Blood culture. Bacteriologic culturing of blood samples should be obtained during febrile episodes before antibiotic administration. Some veterinarians recommend that three blood samples be collected from different sites during a 2-hour period at least 24 hours after the last dose of antibiotics (if administered empirically) or before antibiotic therapy has been initiated.

(2) Echocardiography (M-mode and 2D) may show evidence of a vegetative lesion on the heart valves. The lesion must be at least 2–3 mm in diameter in order to be seen. This test may be less sensitive but more specific than a blood culture.

e. Differential diagnoses

(1) In animals with signs of left-sided heart failure, differential diagnoses include respiratory disease and other diseases causing pulmonary edema (e.g., diseases associated with hypoproteinemia).

- (2) In cattle with signs of right-sided heart failure, the following conditions must be ruled out:
  - (a) Septic pericarditis, often a sequela of traumatic reticuloperitonitis
  - (b) **Cor pulmonale**, an effect of lung dysfunction on the heart
  - (c) Cardiac **lymphosarcoma**, an uncommon sequela of bovine leukemia virus (BLV) infection
- f. Therapeutic plan. Treatment decisions must take into account the economic value of the animal, the cost of treatment, the owner's emotional attachment to the animal, and the prognosis.
  - (1) Antibiotic therapy must be aggressive and lasts for weeks to months. Bactericidal antibiotics are chosen on the basis of sensitivity patterns and the ability of the drug to penetrate tissue. After completion of therapy, follow-up blood cultures should be performed at least once during the next 60 days. If the cultures are positive, antibiotics must be administered again.
  - (2) Treatment of specific organ dysfunction may be required. The use of anticoagulants to prevent emboli has not been thoroughly investigated in horses.
- g. Prognosis
  - (1) Horses. Survival rates in horses with BE have not been reported, but the prognosis appears to be grave.
  - (2) Swine. Mortality surveys of sows indicated BE to be the cause of death in 6.4%–8.6% of cases.
  - (3) Cattle. Prognosis is poor to grave.

### C. Jugular thrombophlebitis (JT). Thrombosis is the formation of a clot that obstructs blood flow.

1. Patient profile. JT can occur in any large animal species. Most affected animals have a history of recent jugular venipuncture or catheter placement. JT occurs most commonly in horses treated for acute toxic enteritis or colitis.
2. Clinical findings include a noticeable enlargement or mass associated with the jugular vein. The mass may be warm, red, or painful. Sometimes the jugular has a rope or cord-like appearance. Edema and venous congestion of the area drained by the affected vein may also occur, leading to swelling of the head. Pyrexia, inappetence, and depression may be present.
3. Etiology and pathogenesis
  - a. Etiology. The specific causes of JT are unknown. Possible causes of JT include trauma (intimal damage), venous stasis, and catheterization.
    - (1) Iatrogenic factors may predispose an animal to JT by causing intimal damage subsequent to placement of a jugular catheter. These factors include the length of time the indwelling catheter has been in place; the site and technique of venipuncture; the composition, contamination, and pH of infusates; the thrombogenicity of catheter material, and the diameter and length of the catheter.
    - (2) **Hypercoagulable** states may lead to JT without intimal damage. These states include dehydration, endotoxemia, anemia, hypotension, stress, or venous stasis.
  - b. Pathogenesis. Irritation of the intimal lining of the jugular vein, stasis of blood, and/or the existence of a hypercoagulable state trigger the clotting cascade and lead to the development of thrombosis. Blood flow is occluded because of the restricted lumen size. Secondary thrombosis can result from perivascular inflammation caused by cellulitis, lymphangitis, or other sources of bacterial invasion around the blood vessels. In severe cases, septicemia leading to endocarditis or pneumonia may occur.
4. Diagnostic plan and laboratory tests
  - a. Ultrasound may reveal cavitating lesions involving the jugular vein. An echodense thrombus with an anechoic area in the center and restricted blood flow may be seen.
  - b. Cultures. A needle aspirate of blood and fibrin can be obtained for culture. An ul-

trasound can be used to identify fluid pockets and guide the placement of the needle into them to obtain an aspirate. The aspirate should be submitted for bacteriologic cultures. The tip of the catheter also can be used for obtaining bacteriologic cultures.

5. Therapeutic plan
  - a. Definitive treatment consists of removal of the catheter if present. Subsequently, the affected vein should not be used for any purpose. Surgical removal or drainage of the affected vein should be considered in animals that are **unresponsive** to medical treatment or those with complications (e.g., bacteremia, toxemia).
  - b. Supportive care
    - (1) Local treatment consists of a hot pack, hydrotherapy, and, in horses, the topical application of dimethylsulfoxide (**DMSO**) or other antiphlogistic salves to reduce local inflammation and increase the blood supply.
    - (2) Broad-spectrum systemic antibiotics are indicated, particularly if cultures are positive. Antibiotic selection should be made on the basis of the bacteriologic culture and a susceptibility study.
6. Prognosis depends on the severity and duration of the problem. Recannulation of the vein can occur over time.
7. Prevention includes:
  - a. Using catheters made out of material with low thrombogenicity (e.g., polyvinyl chloride)
  - b. Placing the jugular catheter high enough in the neck so that the tip is not near the entrance of the anterior vena cava
  - c. Minimizing trauma to the vein during catheter placement
  - d. Maintaining strict asepsis during placement
  - e. Using sterile, particulate-free solutions
  - f. Securing the catheter by suturing it to the skin and covering the site with a sterile antiseptic dressing
  - g. Removing or changing the catheter every 48–72 hours

### D. Aortoiliac thrombosis

1. Patient profile and history
  - a. Patient profile. Although this condition can occur in any large animal species, it is uncommon in all large animal species. In horses, there may be a predisposition for males and certain family lines.
  - b. History
    - (1) In horses, a history of systemic infections (e.g., *Streptococcus equi*, influenza virus), parasites (e.g., *Strongylus vulgaris*), larval migration, back trauma, or racing-associated blood flow turbulence may predispose the animal to aortoiliac thrombosis.
    - (2) In cattle, a history of severe necrotizing colitis and valvular endocarditis may predispose the animal to this disorder.
2. Clinical findings
  - a. Neuromuscular signs include rear limb weakness, paralysis, and exercise-induced weakness or lameness. Trembling and muscle fasciculations and the reluctance to bear weight on the affected limb may be seen. The affected limb is often cooler and drier than the other limbs. Over time, muscle atrophy over the hind quarters occurs.
  - b. Vascular signs. Rectal palpation of the abdominal aorta and its branches (the cranial mesenteric, internal, external, and circumflex iliac arteries) may reveal variations in the amplitude of the pulse and asymmetry. The amplitude of the pulse in the great metatarsal and digital arteries is reduced, and saphenous vein refill time is prolonged, particularly after exercise.
  - c. Pain or anxiety (manifested as elevated heart and respiratory rates and profuse sweating) may be associated with an acute ischemic event. Occasionally, horses show signs of colic.



3. Etiology and pathogenesis
  - a. Etiology. Trauma and infection may be possible causes. Mechanical factors and blood turbulence can lead to intimal tearing.
  - b. Pathogenesis. The most commonly proposed pathogenesis is the detachment of an intracardiac thrombus, which then lodges at the aortic-iliac bifurcation. The condition may be induced by moderate to strenuous exercise.
4. Diagnostic plan and laboratory tests. The thrombus may be visible using 2D ultrasonography if the probe is placed over the terminal aorta per the rectum.
5. Therapeutic plan
  - a. Treatment consists of alternateday aspirin therapy orally and controlled and continued exercise (if nonpainful) to maintain or promote the development of collateral circulation. The development of collaterals requires a significant amount of time.
  - b. Surgery to remove the thrombus is impractical and dangerous.
  - c. Chemotherapeutic agents, such as streptokinase and tissue plasminogen activator, have not been used in large animals.
6. Prognosis. The prognosis is guarded in horses for the return to athletic use. Death may occur in rare cases.

### III. CARDIAC DYSRHYTHMIAS

#### A. Introduction

1. Definition. Cardiac arrhythmias or dysrhythmias are abnormalities in the rate, regularity, or site of origin of the cardiac impulse or a disturbance in the conduction of the impulse.
2. Pacemaker and conductive system. The specialized pacemaker and conductive system of the heart consists of five components. Any disruption in impulse formation, impulse conduction, or both results in arrhythmias. The components include:
  - a. The sinoatrial node, where the cardiac impulse is initiated
  - b. The AV node, where the impulse from the atrium is delayed before passing into the ventricle
  - c. The bundle of His, which conducts the impulse from the AV node into the bundle branches
  - d. The right and left bundle branches, which conduct the impulse into the ventricles
  - e. The Purkinje network, which distributes the impulse to all parts of the ventricle
3. Classification of arrhythmias
  - a. Arrhythmias can be classified in several different ways. Most arrhythmias fit into one of three categories:
    - (1) Autonomic source
    - (2) Cardiac source
    - (3) Extracardiac source
  - b. Regardless of the specific pathologic cause, arrhythmias result from critical alterations in the electrical activity of the myocardial cell.
    - (1) Physiologic arrhythmias. In horses, most arrhythmias are physiologic and are abolished with exercise and excitement. Examples of physiologic arrhythmias include first- and second-degree AV blocks and sinus bradycardia.
    - (2) Pathologic arrhythmias cause poor performance and exercise intolerance. Examples of these arrhythmias include supraventricular arrhythmias (such as supraventricular premature complexes and tachycardia, AF, and advanced second- and third-degree AV blocks).
    - (3) Ventricular arrhythmias are frequently pathologic and include ventricular tachycardia and ventricular premature depolarizations.

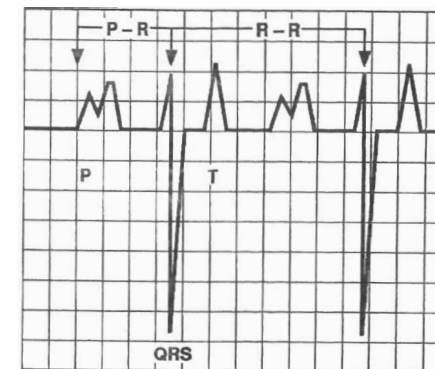


FIGURE 8-1. Enlarged sketch of a normal base-apex electrocardiogram (ECG) from a horse. The P wave, QRS complex, T wave, P-R interval, and R-R interval are indicated. Notice the notched ("M"-shaped) P wave and the absence of a Q wave. Paper speed = 25 mm/sec. Box width = 1 mm.

4. Incidence. It has been estimated that cardiac arrhythmias without any other signs of heart disease may occur in greater than 25% of horses. When accompanied by other cardiac problems, an arrhythmia may occur in as many as 40% of horses.
5. Diagnosis. Evaluation of the ECG involves identifying electrical events that cause characteristic ECG patterns, identifying abnormal patterns, and measuring the rate of occurrence of each pattern. The normal morphology of the patterns varies, depending on the animal and the placement of the ECG leads.
  - a. Waves and complexes. The most basic patterns seen on the ECG tracings are the P wave, the QRS complex, and the T wave (Figure 8-1). Normally, a single P wave is followed within 200–550 milliseconds by a single QRS complex, which is followed within 300–600 milliseconds by a single T wave. These complexes occur closer together in animals with tachycardia and in neonates with high heart rates.
    - (1) The P wave is associated with atrial contraction and is usually a single, short deflection of the ECG. The deflection is usually positive (above the baseline) when using the base-apex lead. Because of the size of the atria in large animals, especially in horses, the P wave may have an "M" shape because the two atria may contract at slightly different times.
    - (2) The QRS complex represents the various waves of depolarization across the ventricles.
      - (a) The Q refers to a negative deflection of the ECG before the first positive deflection and is often absent in large animals.
      - (b) The R refers to the first positive deflection (subsequent positive deflections are referred to as R', R'', and so on).
      - (c) The S (or S, S', and so on) refers to negative deflections after a positive deflection. Hence, a QRS complex may have one Q deflection and multiple R and S deflections.
    - (3) The T wave represents ventricular repolarization. It may be positive or negative and may vary in appearance between successive heart beats.
  - b. Intervals commonly measured are the interval between the beginning of a P wave and the subsequent QRS complex (P-R interval) and the interval between R deflections of successive QRS complexes (R-R interval).
  - c. Interpretation. On a normal ECG, the P wave and QRS complex recur at regular intervals, and have the same appearance each time. Unless two different wave or complex shapes are present on the same lead tracing, it is often difficult to determine that a P wave or QRS complex is abnormal, even if it has an unusual appearance.

- (1) **P waves** with different shapes often suggest that multiple pacemakers are present (**ectopic atrial pacemaker**).
- (2) **QRS complexes.** The occurrence of QRS complexes with different shapes establishes the presence of an **ectopic ventricular pacemaker**, because all supraventricular impulses conduct through the same system and lead to the same QRS appearance. Abnormal QRS complexes frequently are wider than usual, have bizarre appearances, and occur independent of a preceding P wave.
- (3) **Intervals.** The P-R intervals and the R-R intervals should be compared at different areas on the tracing.
  - (a) The **P-R interval** represents the delay in conduction between the atria and ventricles, and can be lengthened by high vagal tone, drugs that slow conduction (i.e., tranquilizers, anesthetics), or pathology.
  - (b) The **R-R interval** represents the heart rate. The occurrence of one or more P waves or QRS complexes before the time predicted by the R-R interval may represent a **premature contraction** or **paroxysmal tachycardia**. Absence of an anticipated beat may represent a **dropped beat**. An abnormal QRS complex that occurs after a prolonged R-R interval is termed an **escape beat**.
- (4) **Calculating the heart rate.** Assuming a standard ECG paper speed of 25 mm/sec, the heart rate (beats/min) = (1500 mm/min)/(number of mm between beats).

## B. Bradyarrhythmias

### 1. First- and second-degree AV block (incomplete block)

- a. **Patient profile.** These conditions are more common in horses and cattle than in small ruminants or swine.
- b. **Clinical findings.** Cardiac auscultation reveals a slow heart rate, an irregular rhythm, and regular S4 that are not associated with S1 or S2.
  - (1) **First-degree AV block** does not cause clinical signs and is unlikely to produce any significant alterations in cardiac function at slow heart rates. Auscultation of animals with first-degree AV block may reveal a separation of S1 and S2 or no abnormalities.
  - (2) **Second-degree AV block.** The jugular pulse may gradually creep up the neck until the beat is conducted. An arterial pulse deficit is palpated. On auscultation, an absence of S1, S2, and S3 is noticed when the block occurs.
- c. **Etiology.** Bradyarrhythmias, such as first- and second-degree AV block, occur because of impaired impulse conduction. The **specific cause** of first- and second-degree AV block is unknown, but it is speculated to be a waxing and waning of vagal tone. The large cardiac mass in horses and cattle may predispose.
  - (1) **Possible causes of first-degree AV block** include cardiac glycosides, quinidine, or procainamide administration, or the presence of hyperkalemia or hypokalemia. Horses may develop the condition in the presence of systemic illness, such as strangles.
  - (2) **Possible causes for second-degree AV block** include infection, xylazine or digitalis administration, electrolyte imbalances, or AV nodal disease. Although AV block can occur in young horses after viral or bacterial infections, only approximately 20% of adult horses with second-degree AV block have an associated infectious disease.
- d. **Diagnostic plan and laboratory tests**
  - (1) **First-degree AV block** is characterized by a normal heart rate, normal P-QRS-T complexes and a prolonged P-R interval (greater than 0.44 seconds in the horse).
  - (2) **Second-degree AV block.** Two types can be distinguished by ECG: **Mobitz type I (Wenckebach)** and **Mobitz type II**.
    - (a) **Mobitz type I** is characterized by a P-R interval that is gradually pro-

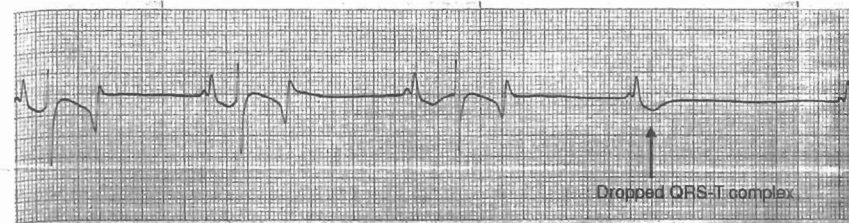


FIGURE 8-2. Base-apex lead-II ECG from a horse with second-degree AV block, Mobitz type I (Wenckebach). Paper speed, 25 mm/sec; 10 mm = 1 mV.

longed until the QRS-T complex is dropped (Figure 8-2). Mobitz type I is the most common type in horses.

- (b) **Mobitz type II** is characterized by a P-R interval that is unchanged, and the blocked beat is unheralded. In both types, the first post-block beat is characterized by a decreased P-R interval, a decreased T-wave amplitude, and a reduction in the negative deflection of the T wave. Sinus arrhythmia frequently accompanies second-degree AV block in horses.

### e. Therapeutic plan and prognosis

- (1) No treatment is required for either AV block. Both of these blocks disappear with exercise.
  - (2) Prognosis is excellent, provided there is no underlying cardiac disease.
2. **Advanced second- and third-degree AV block (complete heart block).** A **second-degree AV block** is considered advanced if it persists with exercise and the heart rate does not increase appropriately in response to exercise, excitement, or atropine. A **third-degree AV block** is characterized by a complete block or isolation of the ventricles from the atria.
    - a. **Patient profile.** These bradyarrhythmias are uncommon in large animals and are associated with severe exercise intolerance and syncope.
    - b. **Clinical findings**
      - (1) **Clinical signs.** Horses with advanced second- and third-degree AV block may show no clinical signs at rest, but they exhibit profound exercise intolerance and lethargy with exercise. Animals with third-degree AV block commonly faint (e.g., animals with **Adams-Stokes syndrome**).
      - (2) **Physical examination findings**
        - (a) **Advanced second-degree AV block.** Cardiac auscultation reveals an absence of S1, S2, and S3 when the block occurs.
        - (b) **Third-degree AV block**
          - (i) The **pulse rate** in horses with this condition is slow (usually 10–20 beats/min), and the **pulse quality** is poor. The heart rate does not increase appropriately in response to exercise, excitement, or atropine.
          - (ii) The **heart rhythm** is frequently regular, but the **intensity** of S1 is variable. The animal often has **high central venous pressure**.
    - c. **Etiology and pathogenesis**
      - (1) **Advanced second-degree AV block.** Underlying cardiac disease is usually present with this block. Chronic inflammatory changes in the AV node and bundle of His have been reported as the causative lesions.
      - (2) **Third-degree AV block.** In this block, the ventricles establish their own rate, which is usually slow (15–20 beats/min). As a result, cardiac output is reduced. The sinoatrial node attempts to compensate and thus, the atrial rate is quite high (94–150 beats/min).
    - d. **Diagnostic plan and laboratory tests**
      - (1) **Advanced second-degree AV block.** Frequently, P waves are not followed by a QRS-T complex. The P-R interval is consistently greater than 0.6 seconds.
      - (2) **Third-degree AV block.** P waves are not associated with QRS-T complexes

and a slower junctional or ventricular escape rhythm is present. The junctional escape rhythm appears as a normal QRS-T complex with a slower rate (20–30 beats/min). A ventricular escape rhythm appears as a QRS-T complex of abnormal morphologic character with a rate of only 10–20 beats/min, which may be uniform or multiform. The P-P interval is regular (Figure 8-3).

e. Therapeutic plan

- (1) Cardiac pacemaker. The definitive treatment of third-degree AV block is the implantation of a cardiac pacemaker, which has been done successfully in a horse.
- (2) Stall rest and treatment with corticosteroids may be beneficial if active inflammation is thought to be present. The administration of dexamethasone to horses with third-degree AV block may result in temporary improvement in third-degree heart block.

3. Sinus arrhythmia, sinoatrial block, and sinus arrest

- a. Patient profile. Sinus arrhythmia is not commonly seen in adult cattle, but it is a frequent occurrence in horses, sheep, and goats. This condition also commonly occurs in young large animals. Sinoatrial block is much less common in horses than incomplete AV block.

b. Clinical findings

- (1) Sinus arrhythmia is characterized by a slow to normal heart rate. There is a cyclic variation in the heart rate that may or may not be associated with the respiratory rate. The heart rate is usually faster during inspiration and slower during expiration. The arrhythmia usually disappears with exercise.
- (2) Sinoatrial block and sinus arrest sound similar to sinus arrhythmia on auscultation.
- (3) Fainting may occur in patients with persistent sinus arrest unless an ectopic pacemaker in the AV junction or in a lower focus takes control of cardiac rhythm. This arrhythmia has not been well documented in horses but has been suspected in some fainting horses with severe atrial myocardial disease.

c. Etiology and pathogenesis

- (1) Sinus arrhythmia is thought to be caused by increased vagal tone. In cattle, this condition may be attributable to acid-base and electrolyte abnormalities as well.
- (2) **Sinoatrial** block occurs when an impulse is initiated in the sinoatrial node but is not conducted to the rest of the heart. This block occurs as an apparently normal phenomenon caused by elevated vagal tone at rest.
- (3) Intermittent sinus arrest is thought to be caused by a reflex increase in vagal tone on inspiration, which leads to an exaggerated sinus arrhythmia. Ocular or carotid sinus pressure may also produce sinus arrest. Other pathologic conditions of the atria, such as dilation and fibrosis, and drug toxicity (e.g., quinidine, digoxin, or propranolol) can cause sinus arrest.

d. Diagnostic plan and laboratory tests

- (1) Sinus arrhythmia. The P-P intervals differ by more than 10%.
- (2) Sinoatrial block is usually diagnosed when a sinus arrhythmia is present in which the P-P interval is at least twice the sinus interval of preceding or subsequent beats. Often, the condition is diagnosed by inference. A type of sinoatrial block has been described in which the P-P intervals become progressively shorter until there is a long pause, and the P-P interval following the dropped beat is prolonged.
- (3) Sinoatrial block cannot be distinguished from sinus arrest when no impulse is initiated from the sinoatrial node, and both atria and ventricles fail to contract.

e. Therapeutic plan

- (1) Sinus arrhythmia requires no treatment.
- (2) Asymptomatic sinoatrial block does not require therapy and usually disappears after exercise or excitement.
- (3) Symptomatic sinoatrial block or sinus arrest may be treated by the administration of atropine or isoproterenol to elevate the sinus rate. If drug toxicity is suspected, the drug should be discontinued.

### C. Tachyarrhythmias

1. Supraventricular tachyarrhythmias

- a. Atrial premature depolarizations (**supraventricular** premature complexes) and atrial tachycardia

- (1) Patient profile. Both of these conditions can occur in all large animal species but are uncommon even in association with cardiac disease. Supraventricular premature complexes occur more frequently than ventricular premature complexes.

(2) Clinical findings

- (a) Affected animals may exhibit no clinical abnormalities or impaired performance and exercise intolerance. The frequency of the premature depolarizations may increase during or after exercise. Other horses may have normal sinus rhythm at rest and develop premature complexes after exercise.

- (b) The heart rate is often rapid, irregularly irregular, and closely resembles AF. With atrial tachycardia, the heart rate is often very rapid (120–220 beats/min).

- (3) Etiology and pathogenesis. Causes of both conditions include increased vagal tone, systemic disease, electrolyte and metabolic disturbances, and myocardial disease. Causes of **myocardial** disease include viruses, bacteria, ischemia, and toxins. Evidence of an underlying cause of the arrhythmia may not be readily apparent.

- (a) Supraventricular tachycardia results from an ectopic focus within the atrium or at the AV junction and may be paroxysmal or sustained. Not all of the atrial impulses are conducted through the AV node and ventricular pathways; thus, second-degree AV block frequently occurs.

- (b) Atrial tachycardia occurs in horses with ventricular pre-excitation (e.g., Wolff-Parkinson-White syndrome). This condition also has been noted during quinidine sulfate therapy for AF and may result from digitalis toxicity or hypokalemia. It may be paroxysmal or continuous.

- (4) Diagnostic plan and laboratory tests. An ECC obtained during exercise may be necessary to determine the clinical relevance of the arrhythmia or to elicit the arrhythmia.

- (a) Supraventricular (or atrial) premature depolarizations. The ECG reveals a premature P wave, often of abnormal morphologic character, which is followed by a normal QRS-T complex. The premature P wave may be buried in the QRS-T complex and, thus, may be difficult to detect. Occasionally, the premature P wave is not followed by a QRS-T complex,

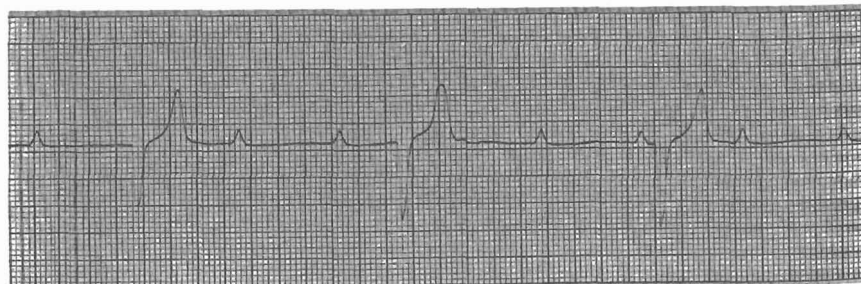


FIGURE 8-3. ECG recorded from a horse with third-degree AV block. Paper speed, 25 mm/sec; 10 mm = 1 mV.

TABLE 8-3. Digoxin Treatment Protocol for Horses and Cattle with Congestive Heart Failure (CHF)

Digoxin Dose	Horse	Cow
Priming dose	12–14 $\mu\text{g/kg}$ intravenously 34 (elixir)–70 (tabs) $\mu\text{g/kg}$ orally	22 $\mu\text{g/kg}$ intravenously
Maintenance dose	6–7 $\mu\text{g/kg/24 hr}$ intravenously 17 (elixir)–35 (tabs) $\mu\text{g/kg/24 hr}$ orally	Infusion of 0.86 $\mu\text{g/kg/hr}$ intravenously 11 $\mu\text{g/kg}$ intravenously every 8 hours

particularly if the impulse occurred early in diastole and arrives at the AV node before the tissue has completely depolarized.

- (b) Atrial tachycardia. The conformation of P waves is different from those seen during normal sinus rhythm. Because not all atrial impulses are conducted through the AV node and ventricular pathways, second-degree AV block may be present, making the diagnosis of the arrhythmia from the ECG difficult. Paroxysmal bursts of tachycardia are four or more premature beats, starting and ending abruptly and lasting less than 30 seconds. The RR interval is usually regular.
- (5) Therapeutic plan
  - (a) Identification and removal of the primary cause is important in the treatment of both arrhythmias.
  - (b) Stall rest for 1–2 months with frequent monitoring of heart rate and rhythm is recommended in horses.
  - (c) **Digoxin** (Table 8-3). If supraventricular tachycardia is sustained and results in CHF, treatment with digoxin may help slow the ventricular response to the atrial impulse. Application of pressure to the eye or carotid sinus before and after digitalization may help decrease the heart rate.
  - (d) Quinidine sulfate may be effective because it suppresses the ectopic foci and prolongs the refractory period of the atrial musculature.
  - (e) Treatment with **corticosteroids** has been suggested but is controversial and of questionable efficacy.
  - (6) Prognosis depends on the underlying problem and the ability to correct the arrhythmia.
- b. AF in horses
  - (1) Patient profile. AF occurs in most horse breeds, but the condition appears to be particularly common in young male Standardbreds and draft horses. This apparent breed and sex predilection is probably a reflection of the equine population in areas where studies were conducted. Reports of AF in ponies, yearlings, and foals are rare. AF is the most common arrhythmia affecting equine athletes.
  - (2) Clinical findings
    - (a) Clinical signs are variable.
      - (i) **Broodmares** and horses doing light work are generally asymptomatic, and AF is an incidental finding.
      - (ii) Performance horses with AF usually are exercise intolerant and may exhibit exercise-induced pulmonary hemorrhage (EIPH), dyspnea, myositis, ataxia, or collapse after exercise.
      - (iii) Horses with moderate to severe left or right AV valvular regurgitation may have signs of CHF, in addition to AF.
      - (iv) Horses presenting with colic occasionally have concurrent AF, but generally AF is not associated with gastrointestinal disease in horses.
    - (b) Cardiovascular examination is abnormal in affected horses.
      - (i) Characteristic findings. An irregularly irregular cardiac rhythm, vari-

able intensity heart sounds, and the absence of S4 are characteristic findings on cardiac auscultation.

- (ii) The resting heart rate is usually normal, but heart rates may range from less than 20 to more than 60 beats/min. Heart rates that are more than 60 beats/min generally indicate underlying heart disease and CHF, whereas extremely slow rates suggest an underlying conduction disorder.
- (iii) Pulse pressures in affected horses may vary from beat to beat.
- (iv) Systolic heart murmurs, consistent with mitral or tricuspid insufficiency, are common.
- (3) Etiology and pathogenesis. AF is thought to be initiated by an atrial premature depolarization and sustained by a reentry mechanism. Variation in the ability of adjacent areas of atrial myocardium to be depolarized by an aberrant impulse (inhomogeneous refractoriness) is required for reentry to occur.
  - (a) AF in the absence of underlying cardiac pathology. The large atrial mass and high vagal tone of normal horses are predisposing factors for the development of AF.
    - (i) A large atrial myocardial mass promotes reentry because it increases the likelihood that an aberrant impulse will encounter a **nonrefractory** myocardium.
    - (ii) High vagal tone shortens the effective refractory period and increases inhomogeneous refractoriness, thereby further promoting reentry.
  - (b) AF in the presence of underlying cardiac disease
    - (i) Focal **myocardial** diseases (e.g., myocarditis) can cause physical heterogeneity of atrial myocardial fibers and may allow AF to persist.
    - (ii) Acquired or congenital cardiac diseases that result in atrial enlargement promote the reentry of aberrant impulses and maintain AF. Moderate to severe left AV valvular insufficiency causes atrial enlargement and has been documented in 10%–84% of horses with AF.
  - (c) AF and potassium depletion. Decreased atrial myocardial cell potassium content may contribute to the development of AF. Potassium loss in sweat and the use of **potassium-depleting** drugs (e.g., furosemide) cause potassium depletion in horses.
  - (d) Paroxysmal AF, an arrhythmia that occurs during maximal exercise and resolves within 24 hours, has been associated with transient poor performance in horses.
    - (i) Rapid pacing of the atria during exercise can cause paroxysmal AF.
    - (ii) Paroxysmal AF occurs occasionally in horses with gastrointestinal **disorders** and in horses under general anesthesia.
    - (iii) Potassium depletion may also be cause of paroxysmal AF.
- (4) Diagnostic plan and laboratory tests
  - (a) **ECG** findings
    - (i) An irregular **R-R** interval with the absence of P waves and coarse baseline f waves is diagnostic of AF (Figure 8-4).
    - (ii) Some variation in QRS and T morphology may be noted.
    - (iii) Occasionally, horses will have ectopic ventricular depolarizations, which appear as bizarre shaped or widened QRS complexes.
  - (b) Echocardiographic findings. Echocardiography should be performed to detect underlying cardiac disease, such as atrial enlargement or severe valvular regurgitation in horses with auscultable murmurs.
  - (c) Clinical pathology
    - (i) Urinalysis. Urinary fractional excretion of potassium can be measured to assess the **whole-body** potassium status.
    - (ii) Cardiac **isoenzyme activities** can be determined if an underlying myocarditis is suspected.
- (5) Therapeutic plan
  - (a) Quinidine, a negative inotrope and positive chronotrope, is the drug of

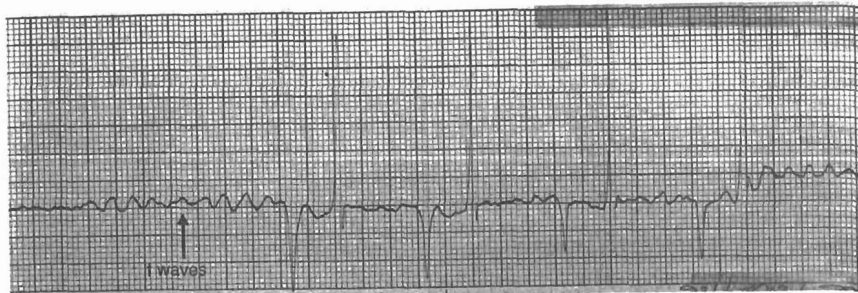


FIGURE 8-4. Base-apex lead-II ECG from a horse with atrial fibrillation. Paper speed 25 mm/sec; 10 mm = 1 mV. Notice the absence of P waves and the presence of flutter waves with irregular rhythm; heart rate = 30 beats/min; 10 mm = 1 mV.

choice for treatment of AF in horses. It prolongs the effective refractory period of the atrial myocardium, thereby suppressing reentry.

(i) Side effects

- Quinidine has **anticholinergic** properties that promote AV nodal conductivity and cause tachycardia. This drug should not be used alone in horses with tachycardia (i.e., horses with a heart rate greater than 60 beats/min) or CHF. Concurrent digoxin therapy is required to support the failing heart of such patients.
- Quinidine has  **$\alpha$ -adrenoreceptor** blocking properties, which can cause vasodilation and hypotension in treated patients.

- (ii) Administration. There are several protocols for quinidine administration in horses, including intravenous and oral regimens with or without digitalization (Table 8-4). Oral dosing requires **nasogastric intubation** because direct oral administration causes oral ulceration.

(iii) Pharmacokinetics

- Quinidine concentration peaks  $\pm$  2 hours after oral administration.
- Quinidine is 80% protein-bound in plasma and undergoes hepatic metabolism and urinary excretion. In horses, the drug's half-life is  $\pm$  6 hours.
- Therapeutic index. Quinidine has a narrow therapeutic index. **Therapeutic plasma** concentrations range from 2 to 4  $\mu\text{g/ml}$ . Signs of toxicosis occur at plasma concentrations of more than 5  $\mu\text{g/ml}$ . Ideally, quinidine concentrations in plasma should be monitored during therapy, and treatment intervals should be adjusted to maintain concentrations in the therapeutic range.

- (iv) Drug monitoring for quinidine toxicosis. Because drug monitoring is impractical in many instances, horses undergoing treatment are closely monitored for ECG changes or clinical signs that may indicate quinidine toxicosis. For horses undergoing intravenous quinidine treatment, continuous ECC monitoring is preferred and is essential. Horses that are administered quinidine orally should have an ECC performed every 2 hours (i.e., immediately before the next treatment and at the peak plasma concentration). Signs indicating quinidine toxicity and the appropriate actions are described in Table 8-5.

(b) Treatment of CHF

- (i) Diuretics. The main treatment includes diuretics (e.g., furosemide), vasodilators, and positive inotropic agents (e.g., digoxin; see Table 8-3).

TABLE 8-4. Quinidine Treatment Protocols for Horses with Atrial Fibrillation (AF)

Description	Protocol	Indications
Quinidine gluconate IV	With continuous ECC monitoring, administer 1.0–1.5 mg/kg quinidine gluconate IV over 1 minute and repeat every 5–10 minutes until sinus rhythm is restored. Stop treatment when (1) a total dose of 11 mg/kg has been administered; (2) the QRS complex duration increases to $>25\%$ over baseline; or (3) tachycardia ( $>90$ beats/min) and/or other clinical signs of toxicity are observed.	Horses with AF of $<1$ week's duration and no evidence of underlying cardiac disease are candidates for this regimen.
Quinidine sulfate PO (standard protocol)	Administer 22 mg/kg quinidine sulfate via nasogastric tube every 2 hours until sinus rhythm is restored. Stop treatment when (1) 6 treatments of 22 mg/kg each (a total dose of 132 mg/kg) have been given; (2) the QRS complex increases to $>25\%$ of baseline; or (3) tachycardia ( $>90$ beats/min) and/or other signs of quinidine toxicity are observed. This procedure can be repeated for 3 consecutive days.	Horses with AF of $\leq 4$ months' duration and no evidence of underlying cardiac disease are candidates for this regimen.
Quinidine sulfate PO (modified protocol)	This protocol is similar to the standard protocol. If sinus rhythm is not restored after 4–6 treatments of 22 mg/kg each, treatment intervals are increased to once every 6 hours to maintain steady-state plasma concentrations. These treatments every 6 hours are usually continued for 2 days.	Horses with AF of long duration, or with significant underlying cardiac disease but no evidence of CHF, are candidates for this regimen.
Quinidine sulfate PO followed by digoxin PO	If conversion with the modified protocol has not occurred by day 2 oral digoxin at 0.01 mg/kg every 12 hours should be added to the treatment regimen.	Horses with AF of long duration, or with significant underlying cardiac disease with or without CHF, are candidates for this protocol.

CHF = congestive heart failure; ECC = electrocardiogram; IV = intravenously; PO = orally.

- (ii) Exercise restriction and dietary sodium reduction are important.
- (iii) Intravenous fluid support is necessary for the correction of dehydration and electrolyte and acid–base imbalances.

(6) Prognosis

- (a) In the absence of underlying cardiac disease, AF is treated successfully in 90% of cases. Clinical findings that indicate a good prognosis include:
- (i) Duration of exercise intolerance less than 4 months
  - (ii) Intensity of cardiac murmur less than grade III
  - (iii) Resting heart rate less than 60 beats/min
  - (iv) No evidence of CHF
- (b) Several factors have been associated with the lack of conversion, recurrence of the arrhythmia, or signs of quinidine toxicity. These include:
- (i) A prolonged (i.e., greater than 4-month) history of poor performance
  - (ii) Intensity of cardiac murmur greater than grade III
  - (iii) Resting heart rate greater than 60 beats/min
  - (iv) Signs of CHF

## c. AF in cattle

(1) Patient profile. AF is diagnosed most often in mature, hospitalized dairy cattle. The fact that AF is diagnosed more frequently in dairy cattle than beef cattle reflects the prevalence of dairy cattle in hospital populations where studies were conducted, not necessarily a breed predisposition.

## (2) Clinical findings

## (a) Extracardiac signs

- (i) Cattle with AF generally have evidence of gastrointestinal disease (e.g., abomasal displacements, indigestion, diarrhea). AF has also been associated with foot rot and pneumonia in cattle.
- (ii) Anorexia and decreased milk production are common in cows with AF and are likely secondary to underlying gastrointestinal problems.

## (b) Cardiovascular signs

- (i) Heart rate. Affected cows have an irregular heart rhythm with no underlying regularity. Heart sounds vary in intensity, and S4 is absent. Heart rates may be slow, normal, or fast; tachycardia in cattle usually is associated with serious underlying gastrointestinal disease.
- (ii) Arterial pulses vary in intensity, but actual pulse deficits are rare.
- (iii) Heart murmurs and sign of CHF are extremely rare in cattle with AF.

(3) Etiology and pathogenesis. The pathogenesis of AF in cattle is the same as in the horse. Predisposing factors include:

- (a) Gastrointestinal diseases, such as displaced abomasum, vagal indigestion, or diarrhea
- (b) Myocardial or cardiac diseases, such as myocarditis, BE, cardiomyopathy, or traumatic reticulopericarditis
- (c) Vagal nerve irritation (such as may occur with severe respiratory disease)
- (d) Organic brain disease (e.g., thiamine-responsive encephalopathy), which can cause sympathetic or parasympathetic stimulation
- (e) Electrolyte disturbances, such as hyper- or hypocalcemia or acid-base imbalances, such as metabolic alkalosis

TABLE 8-5. Quinidine Toxicity in Horses

Finding	Action
Cardiac signs	
Prolongation of the QRS complex to >25% of the pretreatment value	Stop treatment.
Sustained increase in ventricular rate of >100 beats/min	Add digoxin (0.002 mg/kg IV; 0.01 mg/kg PO) to slow the ventricular rate.
Severe atrial tachycardia (rare)	Stop treatment. Administer isotonic sodium bicarbonate (1 mmol/kg) to increase protein binding of quinidine. Administer digoxin (0.002 mg/kg) to slow the ventricular rate. Rapidly infuse isotonic fluid to expand plasma volume. Administer a pressor agent [e.g., phenylephrine (10 mg in 500 ml of 0.9% saline as a fan drip)]
Extracardiac signs	
Depression, paraphimosis, colic, diarrhea, laminitis, upper airway edema, ataxia, convulsions, and urticaria	Stop treatment and address individual problems. If colic is mild, quinidine therapy can be continued. Flunixin meglumine may be used to control abdominal discomfort.

IV = intravenously; PO = orally.

- (f) Other inflammatory or infectious conditions, such as foot rot causing pain-mediated vagal disturbance
- (4) Diagnostic plan and laboratory tests
- (a) An ECG tracing is required for definitive diagnosis of AF. ECG changes in cattle are similar to those described for horses [see III C 1 b (4) (a)].
  - (b) Echocardiography should be performed if underlying cardiac disease is suspected. However, in most cases, this test is not necessary.
  - (c) Serum analysis
    - (i) A serum biochemical profile and blood gas analysis should be performed to detect electrolyte and blood gas abnormalities. Electrolyte and blood gas disturbances, which are common in cattle with AF, are attributable to underlying gastrointestinal disease. Multiple electrolyte derangements in the same individual and high vagal tone associated with gastrointestinal disease may be important in establishing AF in cattle.
    - (ii) Metabolic alkalosis is the most consistent finding. Hypokalemia, hypochloremia, and hypocalcemia also may be present.
- (5) Therapeutic plan
- (a) Treatment of the primary gastrointestinal problem and the correction of electrolyte balance in cattle with AF often result in spontaneous conversion to normal sinus rhythm, usually within 5 days.
  - (b) Quinidine therapy
    - (i) Indications. Quinidine therapy is indicated for cattle that do not convert spontaneously within 5 days, cattle with chronic gastrointestinal problems (e.g., vagal indigestion), and cattle with low cardiac output secondary to AF (e.g., those with poor peripheral perfusion, weak arterial pulses, pulse deficits).
    - (ii) Administration. Quinidine sulfate (48 mg/kg suspended in 4 L of isotonic saline or lactated Ringer's solution) is administered at a rate of 1 L/hr while intravenous fluids are administered simultaneously in the opposite jugular vein. The ECG should be monitored frequently during the infusion and the infusion discontinued as soon as conversion occurs. Therapy should be discontinued after the 4-L infusion, even if the cow still has AF.
    - (iii) Monitoring and side effects. Cattle should be closely monitored during the infusion. Diarrhea and depression are common side effects, and the infusion can be continued despite their occurrence. The infusion rate should be slowed if the ventricular rate is more than 100 beats/min or if the QRS complex is visibly prolonged.
  - (c) Digoxin is used before quinidine therapy in cattle with heart rates greater than 100 beats/min (see Table 8-3).
- (6) Prognosis
- (a) The prognosis for cattle with AF is good if spontaneous conversion occurs after the correction of the primary problem. Unless underlying heart disease is present, few cattle revert to AF.
  - (b) In rare cases, cattle do not respond to quinidine therapy. These unresponsive animals generally have progressive cardiac disease and are poor producers.
2. Ventricular tachyarrhythmias. Generally, ventricular arrhythmias are less common than atrial arrhythmias in large animals and are more indicative of cardiac disease.
- a. Ventricular premature depolarizations and tachycardia
- (1) Patient profile. Intermittent or persistent ventricular tachycardia is very uncommon in large animals.
  - (2) Clinical findings. Common clinical signs include fever, exercise intolerance, weight loss, anorexia, and lethargy.
    - (a) Ventricular premature contractions may be detected by auscultation and palpation of the pulse.

- (i) Heart rate. The beats occur earlier than expected and are usually followed by a pause.
- (ii) Heart sounds. A loud diastolic summation sound with a S2 of variable intensity may be heard. The peripheral pulse and S2 may even be absent during the premature beats. After a normal beat, only S1 and S2 are heard immediately. This sound differs from a normal S3, which can be heard in some horses, because it is usually louder and more prolonged.
- (b) Ventricular tachycardia generally is defined as four or more sustained ventricular depolarizations occurring at a rapid rate. With this disorder, the heart rate is **rapid and regular**. Periods of tachycardia may vary by **starting and stopping suddenly**, lasting for four or more beats, or persisting for hours or weeks.
- (3) Etiology
  - (a) Causes in horses include septicemia or toxemia, severe digestive disturbances, and primary cardiovascular disease characterized by myocardial damage.
  - (b) Predisposing factors. Various drugs (e.g., inhalant anesthetics), toxins, and electrolyte disturbances increase myocardial irritability and may exacerbate premature ventricular beats, which are thought to be caused by interference with the conduction of impulses originating from the same focus. Hypoxia, anemia, uremia, acidosis, sepsis, hypokalemia, and exhausting exercise are predisposing factors.
- (4) Diagnostic plan and laboratory tests
  - (a) ECG
    - (i) Ventricular premature **contractions** are characterized by the presence of wide, bizarre-shaped QRS complexes that appear earlier than expected and are not preceded by a true premature P wave. The T wave is usually oriented in the opposite direction to the QRS complex. A normal P wave occurs at its expected time but may not be evident if it is buried within the QRS-T complex of the premature systole. The interval between the end of the previous T wave and the beginning of the premature QRST complex is usually constant. Two or more different shapes of QRS complexes and different R-R intervals suggest that several different ectopic foci are inducing the contractions. Ventricular fusion beats may be apparent. These beats occur if the ventricular ectopic pacemaker initiates an impulse after the impulse from the normal pacemaker has already entered ventricular tissue. As a result, the ventricle is excited from **two** sources, and a QRST complex is created with an appearance intermediate between that of the premature systole and the dominant beat.
    - (ii) Ventricular tachycardia produces a series of QRST complexes that are bizarre in contour. Sometimes P waves occur independently at a slower rate than the ventricular complexes. Ventricular fusion beats may be present. Bidirectional ventricular tachycardia is characterized by alternate QRS complexes that occur in opposite directions.
  - (b) Echocardiography may be useful to look for myocardial, endocardial, or valvular damage to the heart. It may be normal.
- (5) Therapeutic plan. Therapy for both arrhythmias should be initiated immediately and should be directed toward the underlying condition, which may be CHF, neoplasia, pericarditis, myocarditis, or secondary problems (e.g., hypoxia, uremia).
  - (a) The correction of acid-base and electrolyte **disturbances** should be attempted. Rest, nonsteroidal anti-inflammatory drugs (NSAIDs), and Systemic antimicrobials are often indicated.
  - (b) Digitalis. The use of digitalis for ventricular premature systole and ventricular tachycardia may eliminate the ventricular ectopic contraction. This agent can be used if the patient has CHF.
  - (c) Lidocaine hydrochloride (0.5–1.0 mg/kg intravenously) may be helpful

- for arresting ventricular premature beats in situations other than cardiac failure. However, lidocaine may cause twitching and convulsions in unanesthetized horses.
- (d) Quinidine sulfate can be used to treat both of these arrhythmias.
  - (i) Doses are 20 mg/kg orally every 6 hours until conversion or 6 mg/kg intravenously at a rate of 0.5 mg/kg/hr.
  - (ii) Side effects. This drug can result in hypotension and reduced myocardial contractility.
- (e) Magnesium sulfate supplementation has been used successfully in the treatment of ventricular tachycardia in horses.
- (6) Prognosis is guarded. Ventricular tachycardia is particularly dangerous because it may convert to ventricular fibrillation and cause death.
- b. Ventricular fibrillation is frequently the immediate cause of death in moribund animals. Transient ventricular fibrillation is not known to occur in large animals.
  - (1) Clinical findings. Ventricular fibrillation is so rapidly fatal that it is rarely detected clinically except in animals under anesthesia. Few if any clinical signs occur before death. Cardiac auscultation may reveal a complete, sudden cessation of heart sounds. A pulse is absent, and there is a precipitous drop in blood pressure.
  - (2) Etiology and pathogenesis
    - (a) Etiology. Causes are the same as those for ventricular premature beats and ventricular tachycardia [see III C 2 a (3) (a)]. Ischemic damage to the heart is usually the underlying cause of this arrhythmia.
    - (b) Pathogenesis. Coordinated contraction of the ventricles ceases with this arrhythmia, and continuous chaotic activity replaces regular systole and diastole.
  - (3) Diagnostic plan and laboratory tests. ECG reveals bizarre, irregular oscillations without normal QRS-T complexes.
  - (4) Therapeutic plan. No treatment is currently available.
    - (a) Electrical defibrillation of adult large animals, such as horses and cattle, has not been successful with available equipment.
    - (b) Some work in humans and primates has shown dietary enrichment with fish oil-derived omega-3 polyunsaturated fatty acids (to suppress ventricular fibrillation) to be beneficial.

## IV. PERICARDIAL DISEASE

### A. Introduction. Pericardial diseases are rare in veterinary species.

1. Etiology. There are several reported causes for pericardial disease in large animals, which can be grouped as congenital and acquired. Acquired pericarditis is more common. Causes include bacterial and viral infections, neoplasia, and trauma. Idiopathic pericarditis is also widely reported.
2. Pathogenesis
  - a. Pericardial disease causes diastolic cardiac dysfunction with minimal alterations in systolic function. Elevated intrapericardial pressure inhibits diastolic cardiac filling, resulting in a reduction in preload for a given venous filling pressure. As a result of the reduction in preload, there is decreased cardiac output if there are no compensatory changes in heart rate, cardiac contractility, and vascular resistance.
  - b. Pericardial effusion and constrictive pericarditis are the two major pathologic consequences of pericarditis. As the pericardium accumulates fluid or the wall of the pericardial sac becomes thickened, the stretching limit of the pericardial sac is exceeded, and pressure in the pericardial cavity begins to rise. Cardiac tamponade occurs when pericardial pressure exceeds the cardiac filling pressures, causing diastolic filling to be impaired.



**B.** Pericarditis in cattle

1. Patient profile. Pericarditis is uncommon in cattle, but when it occurs, it usually affects adult cattle and typically lasts 1 week or more. Traumatic pericarditis occurs in less than 10% of cattle with traumatic reticuloperitonitis. This pericarditis often occurs in adult cattle during late gestation or early postpartum.
2. Clinical findings
  - a. **Complaints** may include weakness, anorexia, weight loss, and depression.
  - b. **Physical examination findings**
    - (1) Hyperpnea, prominent scleral vessels, fever, and signs of right-sided CHF (e.g., distended jugular and mammary veins; jugular pulsations; mandibular, brisket, and ventral edema; weak peripheral pulses) are usually present.
    - (2) Auscultation of the thorax often reveals tachycardia and muffled heart sounds, with fluid auscultable in the region of the heart. Lung sounds may be absent in the ventral thorax.
    - (3) **Rumen** motility is generally decreased. Signs of cranial abdominal pain are usually present, as well as a reluctance to move.
3. Etiology
  - a. Trauma is a common cause of pericarditis in cattle. Trauma may be induced by external wounds, the penetration of ingested foreign objects, the hematogenous spread of infection (e.g., septicemia), or the extension of infection from other sites, such as the lung, heart, or pleura.
  - b. Other causes. Pericarditis may also result from vegetative endocarditis that affects one or more cardiac valves, CHF, congenital heart defects, toxins, or **neoplasia** (particularly lymphosarcoma).
4. Diagnostic plan and laboratory tests
  - a. Thoracic radiographs of the thorax and cranial abdomen in the standing cow may reveal a gas-fluid interface within the pericardial sac. The heart may assume a large, globoid silhouette. Sometimes a linear metallic foreign body can be visualized in the cranial reticulum, the caudal thorax, or both.
  - b. **Echocardiography** is the most sensitive, specific, and noninvasive diagnostic test. As little as 15–20 ml of pericardial effusion can be seen using M-mode echocardiography. An "echo-free space" is evident between the myocardium and pericardium. The pericardial sac may appear thickened, and poor cardiac contractility is noted frequently.
    - (1) Other cardiac anomalies, such as vegetative valvular lesions or tumors, may be seen on 2D echocardiograms.
    - (2) Evidence of cardiac tamponade, such as right ventricular collapse during diastole and right atrial collapse, are common findings with large effusions.
  - c. Pericardiocentesis can be therapeutic as well as diagnostic. Cytologic, bacteriologic, and viral culturing of pericardial effusion may be done.
    - (1) Technique. Echocardiography is used to guide needle or catheter placement. Usually the procedure is done from the left fifth intercostal space 2.5–10 cm dorsal to the olecranon.
    - (2) Risks. The risks associated with this procedure include laceration of the heart, coronary arteries, or lungs, and the development of ventricular arrhythmias. Care must be taken to avoid contaminating the thorax with septic effusion from the pericardium.
  - d. **Electrocardiography**. An ECG may reveal decreased amplitude of QRS complexes, electrical **alternans** (i.e., altered configuration of the P, QRS, or T complexes), and ST segment elevation or slurring. Some arrhythmias may be present, particularly sinus tachycardia.
  - e. Cardiac catheterization demonstrates an elevation in central venous or right atrial pressure, and the atrial and ventricular pressure curve may appear abnormal. Right atrial, right ventricular, and PA end-diastolic pressures may **equilibrate**.
5. Therapeutic plan and prognosis
  - a. Surgery. Reducing the intrapericardial pressure is the primary goal of treatment.

This can be accomplished by pericardiotomy (surgically opening the pericardial sac) or subtotal pericardiectomy (partially removing the pericardial sac) to facilitate fluid drainage. Other methods of fluid drainage include surgical **marsupialization** (attaching the pericardial sac to the skin wound) or placement of an indwelling surgical drain. At the time of surgery, any foreign body in the thorax can be removed and abscesses can be drained or removed.

- b. Administration of systemic antimicrobials and analgesics may be helpful, as well as lavage of the pericardium. Fluid support, diuretics, and inotropic agents, such as dopamine or digoxin, may be necessary.

**C.** Pericarditis in horses

1. Patient profile. Pericardial disease, in general, is uncommon in horses. It is seen most often in adult horses, although any age can be affected.
2. Clinical findings
  - a. Clinical signs may include fever, jugular distention, poor peripheral pulses, tachycardia, tachypnea or dyspnea, ventral abdominal distention, depression, mild a b dominal pain, syncope, and weakness. Other signs of right-sided heart failure may be present.
  - b. Auscultation of the thoracic cavity often reveals muffled heart sounds, pericardial friction rubs, and suspected pleural effusion. Lung sounds may be dull or absent ventrally, whereas heart sounds may radiate over a wider area.
3. Etiology. There are two major forms of acquired pericardial disease seen in horses: effusive and nonseptic, and exudative, fibrinous, and often septic.
  - a. Idiopathic pericarditis, characterized by an aseptic inflammatory exudate, occurs in horses.
  - b. Bacteria. In several small case series in horses, fibrinous pericarditis was attributed to **Actinobacillus equuli**. This organism is a common inhabitant of the tonsils and fecal contents of normal adult horses and may gain access to the heart hematogenously. Streptococcal infections and **Actinomyces pyogenes** have been associated with individual cases of equine pericarditis.
  - c. **Neoplasia**. A pericardial **mesothelioma** also has been associated with individual cases of equine pericarditis.
  - d. Viruses, such as equine viral arteritis (EVA), equine herpes virus, equine infectious anemia (EIA), and equine influenza, have been suspected but unproven as causes.
  - e. Trauma from external wounds
4. Diagnostic plan and laboratory tests
  - a. The same methods are used in horses as in cattle, although radiography is less sensitive in horses (see IV B 4).
  - b. Laboratory abnormalities include anemia, **leukocytosis**, high fibrinogen and creatinine concentrations, **hyponatremia**, and hyperkalemia.
  - c. Ancillary diagnostic tests. The central venous pressure values exceed 45 cm of water.
5. Differential diagnoses
  - a. **Pleuritis** and pneumonia
  - b. Circumscribed space-occupying lesions in the thorax, such as mediastinal or pulmonary abscess, lymphosarcoma, or invading gamic squamous cell carcinoma
  - c. Spontaneous tears in the atria or rupture of the ascending aorta
  - d. Gunshot wounds
6. Therapeutic plan. Treatment is similar to that in cattle and should be directed at the primary cause (see IV B 5). **Parenteral corticosteroids** and **NSAIDs** may help control idiopathic or nonseptic pericarditis.
7. Prognosis. Relapse and the **deterioration** of the condition can follow short-term improvements. Resolution is unlikely if the adhesive and exudative changes in the thorax are advanced.



- a. Because of poor response to treatment, the prognosis for septic pericarditis is usually guarded to poor.
- b. The prognosis may be fair for idiopathic or nonseptic pericarditis.

**D.** Pericarditis in swine is similar to that in horses and cattle (see IV B, C).

1. Patient profile. Young pigs may be affected.
2. Etiology. Causes include *Streptococcus* species, *Hemophilus parasuis* (Glasser's disease), and *Mycoplasma* species.
3. Diagnostic plan. The diagnosis of pericarditis is often based on postmortem findings rather than radiographs, echocardiography, or ECG monitoring.
4. Prognosis is guarded to poor. Death is usually attributable to septicemia.

## V. MYOCARDIAL DISEASES

### A. Introduction

#### 1. Definitions

- a. Myocarditis is inflammation of the myocardial wall caused by bacterial, viral, or parasitic organisms or thromboembolic disease caused by these organisms. Myocarditis also can occur following bacteremia, septicemia, pericarditis, or endocarditis, regardless of the cause.
- b. Cardiomyopathy is a subacute or chronic disease of the ventricular myocardium that occurs in the absence of valvular disease, congenital malformations of the heart or vessels, or pulmonary disease. In large animals, only dilated cardiomyopathy is important clinically. Dilated cardiomyopathy is associated with ventricular dilation, increased ventricular mass, and decreased systolic function.

#### 2. Patient profile and epidemiology

- a. Patient profile. These diseases have been reported sporadically in all large animal species.
- b. Epidemiology
  - (1) Myocarditis. The prevalence of acute myocarditis is difficult to estimate because the disease often goes undiagnosed, is mild, or is masked by disease involving another organ system. Also, it is difficult to assess the clinical significance of postmortem evidence of myocardial inflammation and fibrosis. Morbidity due to myocarditis is probably underestimated because it is rarely the cause of death and is associated with infectious conditions that manifest themselves in other ways without specific cardiovascular signs.
  - (2) Inherited cardiomyopathy in cattle has an incidence in inbred populations of 3%–5%. These cattle may be linked genetically by the presence of the red gene in Holstein-Friesian cattle. There does not appear to be a sex predilection for this inherited cardiomyopathy.

3. Clinical findings. Some clinical signs are referable to other organ system involvement, including the respiratory system, reproductive tract, gastrointestinal tract, nervous system, or musculoskeletal system. Frequently, animals (particularly pigs) die suddenly with few or no premonitory signs.
  - a. Complaints include depression, weakness, anorexia, intermittent or chronic fever, weight loss, or reproductive failure.
  - b. Physical examination findings include tachycardia with a gallop rhythm, dyspnea, and other respiratory signs.
  - c. Subcutaneous edema of the brisket, ventral thorax, submandibular area, and occasionally the limbs may be noted. Thoracic auscultation may reveal cardiac arrhythmias, murmurs (often either tricuspid insufficiency or a pulmonic valve ejection murmur), or weak or muffled heart sounds.

#### 4. Etiology and pathogenesis

#### a. Etiology

- (1) Myocarditis. The causes of myocarditis vary depending on the species.

##### (a) Cattle

- (i) Bacterial causes include *Hemophilus somnus*, clostridial diseases (e.g., *Clostridium chauvoei*), *Staphylococcus aureus*, and *Mycobacterium* species. *Borrelia burgdorferi*, a spirochete, also may be a cause of myocarditis in ruminants.
  - (ii) Viral causes include the picornavirus that causes foot-and-mouth disease.
  - (iii) Parasitic causes in ruminants include toxoplasmosis, *Neospora caninum*, sarcocystis, and cysticercosis infection.
- (b) Swine. *Staphylococcus aureus*, *Streptococcus suis*, and viruses (e.g., the picornavirus that causes foot-and-mouth disease and the encephalomyocarditis virus) can cause myocarditis in pigs.

##### (c) Horses

- (i) Bacterial causes include *Clostridium chauvoei*, *Streptococcus equi* or zooeidemicus, *Mycobacterium* species, and *Staphylococcus aureus*. *Borrelia burgdorferi*, a spirochete, also may be a cause of myocarditis in horses.
- (ii) Viral causes include EIA, EVA, equine influenza, and the reovirus that causes African horse sickness.
- (iii) Parasitic causes include strongylosis and onchocerciasis.

- (2) Cardiomyopathy. There are several conditions that have been associated with cardiomyopathy, ranging from myocarditis to inherited conditions.

- (a) Cardiomyopathy has been associated with the ingestion of several different chemicals and plants, including ionophores such as monensin and lasalocid, salinomycin, gossypol, *Cassia occidentalis*, and *Phalaris* species.
- (b) Mineral or vitamin deficiencies or excesses have been implicated, including vitamin E and selenium deficiency and primary and secondary copper deficiencies.
- (c) Neoplastic infiltration of the heart by lymphosarcoma or fibrosarcoma may also cause cardiomyopathy.

- b. Pathogenesis. The pathophysiologic changes associated with myocardial disease depend on the specific nature and extent of the disease. Most infectious etiologies cause septicemia and hematogenous spread to the myocardium. Myocardial damage results from either vascular occlusion or direct bacterial, viral, or parasitic action on the myocardium. The end result of myocarditis and cardiomyopathy is reduced myocardial performance (reduced cardiac output).

#### 5. Diagnostic plan and laboratory tests

- a. Clinical pathology. Myocardial tissue can be evaluated by histology and bacteriologic culture.
  - (1) Myocardial enzymes. In animals with acute myocarditis, myocardial enzyme levels, including aspartate aminotransferase (AST), creatine phosphokinase (CK), and lactate dehydrogenase (LDH), are elevated. The sensitivity and specificity of these tests have not been determined for large animals.
  - (2) Analysis of pericardial or pleural fluids reveals a transudate with low protein concentration and predominantly mononuclear cells.
  - (3) Tests for specific diseases may include serology or viral isolation from white blood cells; for bovine leukosis infection, tests for nutritional deficiencies and toxicities, and serum or liver copper concentrations. In horses, serologic testing for influenza, EVA, EIA, and herpesvirus may be helpful.
- b. Echocardiography may show increased ventricular chamber size, decreased thickness of the interventricular septum and left ventricular free wall, and decreased myocardial function. In animals with dilated cardiomyopathy, usually there are increased end-systolic and end-diastolic dimensions of the left and right ventricles, increased left atrial size, and an increased dimension ratio from the left atrium to the aortic root. Mitral valve insufficiency and decreased myocardial function may

be visualized by poor wall motion, which suggests poor contractility. A mass on the right atrium may be seen with BLV-induced lymphoma.

- c. Cardiac catheterization may reveal elevated intracardiac pressures (right atrium, right ventricle, PA, pulmonary capillary wedge, and left ventricular end diastolic) in animals with dilated cardiomyopathy.
6. Differential diagnoses include:
  - a. Other cardiac diseases, such as BE or pericarditis, cardiac neoplasia
  - b. Septicemia or toxemia
  - c. Chronic pneumonia (all large animals) or high-altitude disease (cattle)
7. Therapeutic plan
  - a. Management of myocarditis in all species includes the treatment of the underlying cause (if known) and control of cardiac complications, including dysrhythmias, CHF, or shock.
    - (1) Corticosteroids may be of value in cases of severe toxemia, complicated dysrhythmias, or intractable heart failure.
    - (2) Rest. Performance animals should be rested until signs of systemic illness have resolved and ECG changes have returned to normal.
  - b. Therapeutic management of cardiomyopathy consists of the use of positive inotropes (e.g., digoxin), diuretics, vasodilators, rest, and the drainage of pleural, pericardial, or abdominal fluid.
  - c. Supportive care, including intravenous fluids for the correction of fluid, electrolyte, and acid-base imbalances, NSAIDs, and control of cardiac dysrhythmias are important for successful resolution of myocarditis and cardiomyopathy.
8. Prognosis
  - a. The prognosis for myocarditis is good if there are no signs of heart failure and if cardiac dysrhythmias are managed successfully. The prognosis is guarded to poor if signs of CHF are present.
  - b. The prognosis is poor for animals with dilated cardiomyopathy and BLV-induced lymphoma. Cattle with inherited cardiomyopathy may die by 6 months of age, whereas other animals may be asymptomatic until 2–4 years of age.
9. Prevention and control consist of maintaining good vaccination and parasite control programs. Animals with deficiencies or toxicities should receive adequate concentrations of vitamin E, copper, and selenium in their diets.

**B. Gossypol-induced cardiotoxicosis.** A significant number of cases of gossypol toxicosis have been reported in ruminants in the last few years. This may be due to changes in the methods for extracting oil from cottonseed, increases in the amount of concentrates fed to animals, and the amount of creep feed offered to young ruminants.

1. Patient profile and history
  - a. Patient profile. Young ruminants (e.g., kids, calves, lambs) and monogastrics (e.g., swine) are more susceptible to toxicosis than adult ruminants. The highest death losses have been reported in bottle-fed calves who are fed starter rations that use cottonseed meal as their protein source.
  - b. History. A history of cottonseed in the diet for several weeks to months is necessary for presumptive diagnosis. Often, more than one animal is affected.
2. Clinical findings
  - a. Clinical **signs** may include sudden death, labored breathing, anorexia, stiffness, depression, and occasionally hemoglobinuria. Reproductive problems may be seen in adult ruminants, including sterility in bulls and decreased conception rates in cows. Chronically affected cattle may have decreased heat tolerance, hemoglobinuria, abomasitis, and anorexia.
  - b. Postmortem findings may reveal pulmonary congestion, excessive abdominal, pericardial, and pleural fluid, generalized cardiomyopathy, and chronic passive congestion of the liver (i.e., nutmeg liver).
3. Etiology and pathogenesis
  - a. Etiology. Free gossypol, a yellow pigment that is most concentrated in the seed of

the cotton plant, is the source of toxicity. Gossypol gives the plant its resistance to insects.

- (1) Rations containing either cottonseed meal or whole cottonseed have been associated with gossypol toxicosis.
- (2) Toxicity is influenced by the method of cottonseed processing, dietary concentrations of iron, calcium, and protein, and the presence of other toxic terpenoids and chemicals found in cottonseed. Rations must be fed for a minimum of 1–3 months to cause toxicity.
- b. Pathogenesis
  - (1) The actual mechanism of toxicosis is not known. However, gossypol forms Schiff's base-type derivatives with some amino acids, making them unavailable for protein synthesis, and forms protein–gossypol complexes. Gossypol affects some enzymatic reactions, such as the ability of cells to respond to oxidative stress.
  - (2) Gossypol is primarily a cardiotoxin, causing gradual destruction of the cardiac musculature. It may interfere with cardiac conduction. Adult ruminants are able to detoxify gossypol by binding it to soluble proteins in the rumen and forming stable complexes.
4. Diagnostic plan and laboratory tests
  - a. History and suggestive postmortem and clinical findings are important for diagnosis.
  - b. Feed and tissue analysis for free gossypol concentrations help in diagnosis. Levels of 400 ppm or less free gossypol have been known to cause death in young calves and lambs, whereas older calves and lambs may require levels of 800–1200 ppm.
  - c. Other tests include those listed in V A 5.
5. Therapeutic plan and prognosis. There is no treatment currently available.
  - a. Supportive care may be helpful (see V A 7 a–c).
  - b. Diet. Gossypol should be removed from the diet. Deaths attributable to toxicity may persist up to 2 weeks after the feed is removed. The ability of animals to recover depends on the severity of the heart damage. Most **gossypol-induced** sterility is reversible when the feed is removed.
6. Prevention consists of testing **feed** for free gossypol concentration or avoiding feeding cottonseed meal to animals under 4 months of age. It is possible to dilute the cottonseed by mixing it with other protein **sources**.

#### C. Ionophore-induced cardiomyopathy

1. Patient profile. This disorder affects horses, cattle, and pigs, with horses being the most susceptible.
2. Clinical findings
  - a. Clinical signs include anorexia, stiffness, depression, weakness (especially involving the hind quarters), sweating, ataxia, colic, and recumbency. Congested mucous membranes, **polyuria** progressing to anuria, hematuria, hemoglobinuria, and progressive respiratory distress may be seen. Sublethal doses of ionophores may result in myocardial fibrosis. Signs occur within 12 hours of ingestion, and death may occur 24–36 hours after ingestion.
    - (1) Horses often show **poor** performance, ill-thrift, and subsequent signs of CHF. Chronic exposure in horses may result in profound exercise intolerance.
    - (2) Cattle and sheep may show diarrhea.
    - (3) Pigs may exhibit hypermetria, knuckling, and a reluctance to move.
  - b. Postmortem findings include focal or extensive areas of cardiac muscle pallor and epicardial and endocardial hemorrhages, pulmonary congestion and **serous** effusions compatible with CHF, fibrosis of skeletal muscles, and passive congestion of the liver. Heart lesions in pigs are often confined to the atria.
3. Etiology and pathogenesis
  - a. Etiology

- (1) Toxicoses may result from ingestion by sensitive species of **ionophore-containing** feeds prepared for other species. Mixing errors may result in toxicosis.
- (2) The toxicity of some ionophores is increased by various antibiotics (e.g., tiamulin, oleandomycin, chloramphenicol, erythromycin, sulfonamides) administered concurrently.
- b. Pathogenesis
  - (1) Ionophores form lipid-soluble complexes with cations to facilitate transport of the cations across lipid membranes.
    - (a) The monovalent ionophores are monensin, **salinomycin**, and narasin. They bind sodium and potassium ions, respectively.
    - (b) **Lasalocid** is a **divalent** ionophore that binds divalent cations such as calcium and magnesium ions.
  - (2) Affected muscles
    - (a) Horses. The cardiac muscle is most commonly affected in horses.
    - (b) Ruminants. Cardiac and skeletal muscles are more equally affected in ruminants.
4. Diagnostic plan and laboratory tests
  - a. Serum biochemical findings may include elevated enzyme concentrations such as CK, AST, and alkaline phosphatase, and slight elevations in the concentration of unconjugated bilirubin.
  - b. Hematology. Erythrocyte **fragility** is increased.
  - c. Feed sample analysis (ideally performed on several pounds of feed) may reveal ionophore content. Serum, contents of the gastrointestinal tract, and tissues can also be analyzed, but this analysis is not reliable.
  - d. History, clinical and laboratory findings, and postmortem results may suggest the diagnosis.
  - e. Other tests include those listed in V A 5.
5. Therapeutic plan
  - a. Antidotes for ionophores are not available. Mineral oil or activated charcoal may decrease further absorption.
  - b. Supportive care includes the administration of intravenous fluids to correct electrolyte imbalances, dehydration and shock, diuretics, and stall rest.
6. Prognosis for return to athletic performance is guarded in horses with chronic exposure due to myocardial fibrosis.
7. Prevention of ingestion is the best approach to management.

#### **D. Nutritional cardiac myodegeneration (white muscle disease, mulberry heart disease)**

1. Patient profile. This disease most commonly affects neonates in the first week of life, although it can occur in older animals. In pigs, this disease frequently occurs during the postweaning period (3 weeks to 4 months) and involves rapidly growing pigs.
2. Clinical findings may include dyspnea, cardiac murmurs and arrhythmias, and hemoglobinuria. Affected animals may be weak and exercise intolerant. Death may be immediate as a result of fatal arrhythmias or may occur within a few hours due to exhaustion and circulatory collapse. Other noncardiac signs may include poor reproductive performance (e.g., retained fetal membranes, decreased fertility), ill-thrift, and skeletal muscle weakness or stiffness.
3. Etiology and pathogenesis
  - a. **Etiology**
    - (1) Selenium deficiency. Certain regions of North America are inherently low in selenium. Acid soils, soils originating from volcanic rock, high-sulfur soils, or soils treated with sulfur-containing fertilizers are often deficient in selenium. Forages grown during seasons with heavy rainfall also may be low in selenium.
    - (2) Vitamin E deficiency occurs when animals are fed poor quality hay, straw, or root crops. Stored grain loses its vitamin E content over time.

- b. Pathogenesis. Dietary selenium, sulfur-containing amino acids, and vitamin E act synergistically to protect tissues from oxidative damage.
4. Diagnostic plan
  - a. Clinical pathology
    - (1) Plasma CK and serum **AST** levels often are elevated. The magnitude of increase in these enzymes is directly proportional to the extent of muscle damage. Specific myocardial enzymes [see V A 5 a (1)] may also be elevated.
    - (2) Selenium and vitamin deficiencies. Whole blood, liver, or serum selenium and plasma, liver, or muscle concentrations of vitamin E or  **$\alpha$ -tocopherol** (a vitamin E-containing compound) should be determined.
    - (3) Biopsy. Tissue samples taken by antemortem or postmortem biopsy can be analyzed for concentrations of glutathione **peroxidase** (a selenium-containing enzyme). This enzyme can also be detected in RBCs or platelets.
    - (4) Complete blood cell count (**CBC**). Anemia may be seen on a CBC, particularly in swine. Electrolyte and acid-base imbalances may be present, including hyponatremia, hyperkalemia, and metabolic acidosis.
  - b. Echocardiography. Cardiac lesions can be evaluated by echocardiography (see V A 5 b).
  - c. Soil, forage, and grain concentrations of selenium should be determined.
  - d. Muscle biopsy. Light microscopic changes suggestive of muscle degeneration and acute necrosis include hyaline degeneration, fragmentation, and lysis of muscle cells. There may be evidence of calcification of necrotic muscle (mineralization).
5. Therapeutic plan and **prognosis**
  - a. Therapy consists of parenteral administration of vitamin E or selenium (see also V A 71).
  - b. Prognosis. Animals showing signs of cardiac dysfunction have a poor prognosis. Most animals die within 24 hours.
6. Prevention is aimed at proper supplementation of the dam with vitamin E and selenium either by a salt mix or by total ration supplementation. During late gestation, dams may be given parenteral vitamin E and selenium. In addition, neonates may be given a dose at birth.

## STUDY QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE numbered answer or completion that is BEST in each case.

1. Which grouping correctly describes the heart lesions associated with a tetralogy of Fallot?

- (1) Ventricular septal defect (VSD), right ventricular hypertrophy, overriding aorta, pulmonic stenosis
- (2) Atrial septal defect (ASD), VSD, left ventricular hypertrophy, overriding aorta
- (3) Patent ductus arteriosus (PDA), VSD, right ventricular hypertrophy, pulmonic stenosis
- (4) Tricuspid valve atresia, ASD, VSD, overriding aorta
- (5) Pulmonary vascular truncation, VSD, right ventricular hypertrophy, overriding aorta

2. When is quinidine sulfate most effective for converting atrial fibrillation (AF) to normal sinus rhythm in horses?

- (1) When the resting heart rate is less than 60 beats/min, the duration of AF is 6–10 months, and there are no heart murmurs
- (2) When the duration of AF is 1 year, the horse shows signs of congestive heart failure (CHF), the resting heart rate is 80 beats/min, and there are no heart murmurs
- (3) When there are no signs of CHF, the resting heart rate is 80 beats/min, the heart murmur is less than grade III, and the duration of AF is more than 6 months
- (4) When the duration of AF is less than 4 months, the heart murmur is grade IV, the resting heart rate is 60 beats/min, and there are signs of mild CHF
- (5) When the duration of AF is less than 4 months, the murmur is less than grade III, the resting heart rate is less than or equal to 60 beats/min, and there are no signs of CHF

3. An adult dairy cow develops an irregularly irregular heart rhythm with a rate of 90 beats/min. On physical examination, the veterinarian identifies a left displaced abomasum (LDA). What is the most likely type of arrhythmia and the best treatment?

- (1) Second-degree atrioventricular (AV) block, no treatment is necessary
- (2) Ventricular tachycardia, treated with intravenous lidocaine or digoxin
- (3) Sinus arrhythmia, treated by running the cow around the pen to see if the arrhythmia resolves; if it does, no other treatment is required
- (4) Atrial fibrillation (AF), treated by correcting the LDA and seeing if the arrhythmia resolves in a couple of days
- (5) No arrhythmia is present; cows normally have an irregularly irregular heart rhythm

4. A feedlot in western Canada had several steers that died suddenly with no premonitory signs, often following an episode of pneumonia or meningoencephalitis in the individual or penmates. Postmortem revealed multifocal myocardial infarcts and necrosis and fibrosis with no obvious pulmonary pathology. What is the most likely etiology?

- (1) Bovine leukemia virus (BLV)-associated lymphoma involving the right atrium
- (2) *Haemophilus somnus* myocarditis
- (3) Monensin toxicosis
- (4) An aberrant form of infectious bovine rhinotracheitis (IBR) viral infection
- (5) Shipping fever disease complex involving the *Pasteurella* species

5. A 26-year-old Standardbred mare is examined by a veterinarian before a routine vaccination. The veterinarian hears a grade III, holodiastolic musical murmur on the left side of the chest that radiates toward the apex of the heart. What is the most likely diagnosis and treatment?

- (1) Mitral valve stenosis, no treatment
- (2) Bacterial endocarditis (BE) with a vegetative lesion on the mitral valve, long-term antibiotics
- (3) Pulmonic insufficiency, no treatment
- (4) Aortic insufficiency, no treatment
- (5) Ventricular septal defect (VSD), no treatment

6. What is the most common type of incomplete second-degree AV block in fit racehorses and how it is characterized electrocardiographically?

- (1) Mobitz type II is characterized by a P-Q interval that is unchanged, and the dropped beat (no QRS-T) is unheralded.
- (2) Mobitz type I (Wenckebach) is characterized by a P-R interval that gradually prolongs until the beat (QRS-T) is dropped.
- (3) Mobitz type I is characterized by a P-Q interval that is unchanged, and the dropped beat (no QRS-T) is unheralded.
- (4) Mobitz type II is characterized by a P-R interval that gradually prolongs until the beat (QRS-T) is dropped.
- (5) Mobitz type III (AV dissociation) is characterized by P waves that are completely independent of QRS-T complexes.

7. Several rapidly growing pigs, which were approximately 2 months old, die suddenly. Postmortem examination reveals pericardial effusion, pulmonary and hepatic congestion, and pale discoloration of the grossly enlarged heart. The pigs were fed a diet of soybeans, high-moisture corn, and cereal grain. What is the most likely diagnosis?

- (1) Cardiomyopathy caused by vitamin E or selenium deficiency (mulberry heart disease)
- (2) Bacterial endocarditis (BE) caused by *Erysipelothrix rhusiopathiae*
- (3) Myocarditis caused by the *Sarcocystis* species
- (4) Congenital heart defect such as tetralogy of Fallot
- (5) Atherosclerosis due to a high-fat diet

8. Heart sounds are generated by the:

- (1) impact of valve leaflets coming together.
- (2) snapping open of valve cusps.
- (3) mechanical activity of the heart resulting in sudden acceleration and deceleration of blood.
- (4) turbulent blood moving through incompetent valves.
- (5) contraction and relaxation of the cardiac muscle.

DIRECTIONS: Each of the numbered items or incomplete statements in this section is negatively phrased, as indicated by a capitalized word such as NOT, LEAST, or EXCEPT. Select the ONE numbered answer or completion that is BEST in each case.

9. Which one of the following clinical signs is LEAST likely to be seen in cattle with bacterial endocarditis (BE)?

- (1) Lameness
- (2) Tachycardia
- (3) Heart murmur
- (4) Fever
- (5) Abdominal pain

10. Which one of the following is NOT commonly important in the pathophysiology of pericardial disease?

- (1) Diastolic cardiac dysfunction
- (2) Elevated intrapericardial pressure, causing a reduction in preload
- (3) Systolic cardiac dysfunction
- (4) Decreased cardiac output, assuming heart rate, cardiac contractility, and vascular resistance are unchanged
- (5) Increased sympathetic tone

11. Which congenital heart defect does NOT cause cyanosis and hypoxemia?

- (1) Reverse patent ductus arteriosus (PDA; right-to-left shunt)
- (2) Pentalogy of Fallot
- (3) Ventricular septal defect (VSD) with pulmonary hypertension (right-to-leftshunt)
- (4) Tetralogy of Fallot
- (5) Foramen ovale

12. Which one of the following diagnostic test results could NOT be used to support a diagnosis of white muscle disease?

- (1) Elevated aspartate aminotransferase (AST), creatine phosphokinase (CK), and lactate dehydrogenase (LDH) in serum
- (2) Elevated red blood cell (RBC) glutathione peroxidase activity
- (3) Urinalysis revealing myoglobinuria
- (4) Low selenium concentration in blood
- (5) Skeletal or intercostal muscle biopsy revealing hyaline degeneration and lysis

**DIRECTIONS:** Each set of matching questions in this section consists of a list of four to twenty-six numbered options (some of which may be in figures) followed by several numbered items. For each numbered item, select the ONE numbered option that is most closely **associated** with it. To avoid spending too much time on matching sets with large numbers of options, it is generally advisable to begin each set by reading the list of options. Then, for each item in the set, **try** to generate the correct answer and locate it in the option list, rather than evaluating each option individually. Each numbered option may be selected once, more than once, or not at all.

#### Questions 13–15

Match each valvular defect with the appropriate cardiac auscultation finding.

- (1) **Mitral** regurgitation
- (2) Tricuspid regurgitation
- (3) Pulmonic regurgitation
- (4) Aortic regurgitation

13. Holosystolic murmur with point of maximal intensity (PMI) over the left fifth intercostal space

14. Holosystolic murmur with PMI over the left heart base

15. Holodiastolic decrescendo murmur with PMI over the left fourth intercostal space

## ANSWERS AND EXPLANATIONS

1. The answer is 1 [II A 4]. Tetralogy of Fallot is a cyanotic heart defect that impairs ventricular emptying. This disorder results from an abnormal dextrad (to the right) development of the great vessels. The four components are a ventricular septal defect (VSD), overriding of the interventricular septum by the aorta (overriding aorta), pulmonic stenosis, and right ventricular hypertrophy. If an atrial septal defect is also present, a pentalogy of Fallot exists.

2. The answer is 5 [III C 1 b (5)]. Quinidine sulfate is the drug of choice for conversion of horses with atrial fibrillation (AF) to sinus rhythm and is most successful when the duration of AF is short (less than 4 months), murmurs auscultated are less than grade III–V, the resting heart rate is less than or equal to 60 beats/min, and there are no signs of congestive heart failure (CHF).

3. The answer is 4 [III C 1 c (2), (5)]. Atrial fibrillation (AF) is the most commonly observed arrhythmia in cattle and can be functional or organic in nature. Functional AF develops without apparent cardiac disease and usually is secondary to other clinical problems, such as gastrointestinal disturbances with associated electrolyte disturbances (LDA in this case). AF will frequently convert to normal sinus rhythm without specific treatment. Correction of the LDA will probably result in return to normal sinus rhythm in a few days. Sinus arrhythmia associated with respiration does not normally develop in cattle. The heart rate is usually slow to normal. There may be cyclic variation in heart rate. Ventricular tachycardia suggests underlying cardiac disease. Auscultation usually reveals a rapid but regular heart rate.

4. The answer is 2 [V A 4 a]. *Haemophilus somnus* produces a syndrome consisting of sudden death with few or no premonitory signs, often following an episode of pneumonia or meningoencephalitis. Necropsy of affected animals often reveals multifocal myocardial infarcts, necrosis, and fibrosis typical of embolic disease. *H. somnus*, which is often isolated from these lesions, is an opportunistic pathogen that has a predilection for the bo-

vine female reproductive tract. The septicemic form, which includes myocardial disease, has been increasing in frequency in western Canada since 1987. Lymphoma involving the right atrium occurs infrequently and usually in older animals. Postmortem findings include a mass on the right auricle or within the right atrium, pericardial effusion, and cardiac dilation. Infectious bovine rhinotracheitis (IBR) is not known to cause myocarditis or cardiomyopathy. Pasteurellosis can cause bacteremia and septicemia with resultant cardiac disease, but it usually manifests as a vegetative lesion on one or more cardiac valves, rather than as myocarditis. Pneumonia is also usually present clinically and at postmortem.

5. The answer is 4 [II B 4]. Degenerative changes involving the aortic valve are common in older horses. The murmur associated with aortic regurgitation is holodiastolic, with the point of maximal intensity (PMI) over the aortic valve and radiating toward the left cardiac apex. Aortic regurgitation is usually well tolerated and is not associated with exercise intolerance. Usually, no treatment is necessary. Atrioventricular valve stenosis is rare in horses. Vegetative lesions on the mitral or tricuspid valve may be large enough to cause narrowing of the valve orifice. The associated murmur is a decrescendo diastolic murmur after S<sub>2</sub> and is heard best on the left side of the chest over the mitral valve. Bacterial endocarditis (BE) involving the mitral valve usually results in fever, weakness, anorexia, weight loss, or lameness in addition to the characteristic systolic heart murmur. Pulmonic insufficiency is uncommon in horses. The murmur associated with it is holosystolic with PMI over the pulmonic valve. Usually, horses show other signs of heart disease, such as jugular venous distention and severe exercise intolerance. A congenital heart defect, such as a ventricular septal defect (VSD), produces a holosystolic murmur heard on both sides of the chest.

6. The answer is 2 [III B 2]. Type I Mobitz (Wenckebach) is the most common incomplete atrioventricular (AV) block in horses. It is characterized by progressive lengthening of the P-R interval for several beats until one P wave, representing atrial excitation, occurs

without a subsequent ventricular excitation (QRS-T). The post-block P-R interval is shorter.

7. The answer is 1 [V D]. Mulberry heart disease occurs in rapidly growing pigs, particularly during the postweaning period (3 weeks to 4 months). The pigs are usually fed diets deficient in both selenium and vitamin E. Diets may contain a high concentration of unsaturated fatty acids. Diets commonly associated with the condition include mixtures of soybean, high-moisture corn, and cereal grains grown on soils with low levels of selenium. Without selenium, vitamin E, or both, there is widespread tissue lipoperoxidation leading to hyaline degeneration and calcification of muscle fibers such as myocardial fibers. Myocardial muscle is replaced by fibrosis, leading to pale discoloration and firmness. Bacterial endocarditis (BE) usually involves the left AV valve in pigs. Left heart enlargement and vegetative lesions on the AV valves are seen at postmortem. *Sarcocystis* species cause focal myocarditis, not generalized cardiac discoloration and enlargement. A severe congenital heart defect usually causes clinical signs from birth that progressively worsen with age. Evidence of the cardiac defect would be apparent at postmortem.

8. The answer is 3 [I B 4]. Cardiac sounds originate when the mechanical activity of the heart results in sudden acceleration and deceleration of columns of blood, causing the heart, major vessels, and blood to vibrate as a whole.

9. The answer is 5 [II B 6 b (2)]. The most frequently occurring clinical signs associated with bacterial endocarditis (BE) in cattle include tachycardia, weight loss, lameness, heart murmur, and fever. Colic or abdominal pain is uncommon.

10. The answer is 3 [IV A]. Pericardial disease causes diastolic cardiac dysfunction with minimal if any alterations in systolic function. Elevated intrapericardial pressure inhibits diastolic cardiac filling, causing a reduction in preload for any given venous filling pressure. Reduction in preload results in decreased cardiac output, assuming the heart rate, cardiac

contractility, and vascular resistance are unchanged. The body responds to the decreased cardiac output by increasing sympathetic tone and stimulating the renin-angiotensin-aldosterone system. The elevated sympathetic tone causes elevations in the heart rate and augmentation of cardiac contractility.

11. The answer is 5 [II A 2 c]. Three congenital heart defects result in hypoxemia and cyanosis. They include tetralogy and **pentalogy** of Fallot, right-to-left shunting patent **ductus arteriosus** (PDA), and right-to-left shunting ventricular **septal** defect (VSD). These defects result in the shunting of blood away from the lungs where oxygenation occurs. Chronic hypoxia may lead to progressive secondary **polycythemia** and sludging of the blood. A patent foramen ovale (atrial **septal** defect) usually results in the shunting of blood from the left atrium into the right atrium. This, in turn, results in increased blood volume through the pulmonary circulation. Therefore, hypoxemia is not a common clinical feature.

12. The answer is 2 [V D 4]. Nutritional muscular dystrophy (white muscle disease) may result in elevated muscle enzyme levels [creatine phosphokinase (CK), lactate dehydrogenase (LDH), aspartate **aminotransferase** (AST)], low selenium in serum, low **glutathione** peroxidase activity in blood, and evidence of muscle degeneration on a biopsy. All of these tests are used in conjunction with clinical signs and evidence of low or marginal vitamin E or selenium concentrations in the diet.

13–15. The answers are: 13-1 [II B 2 b], **14-3** [II B 5 b], 15-4 [II B 4 b]. Mitral regurgitation produces a holosystolic murmur that is heard best on the left side with the point of maximal intensity (PMI) in the fifth intercostal space.

Pulmonic regurgitation produces a **holosystolic** murmur that is heard best over the left heart base.

Aortic regurgitation produces a decrescendo diastolic murmur that is heard best on the left side of the chest in the fourth intercostal space. The murmur often radiates over a wide area.